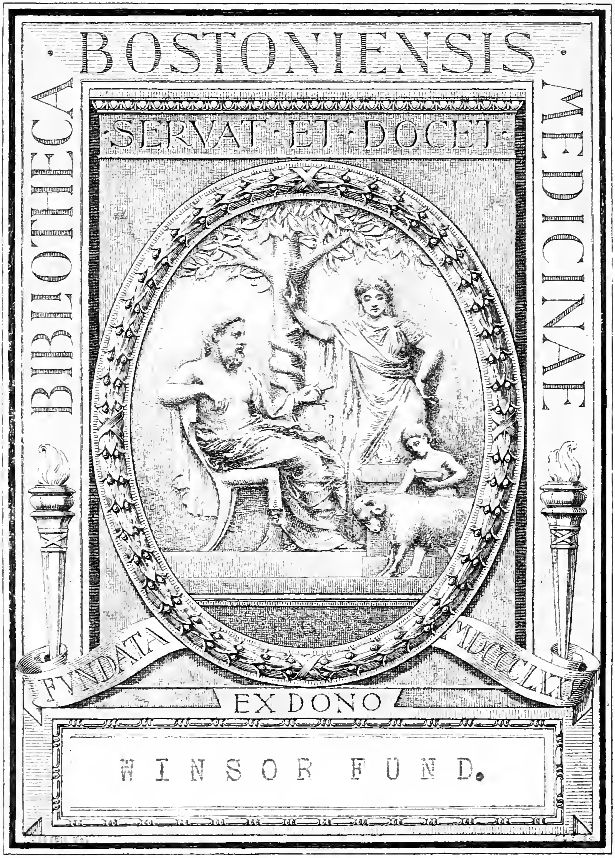
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THE $CHCl_3$-PROBLEM

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$CHCl_3$-PROBLEM

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ANALYSIS

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PREFACE TO VOLUME I.

THE action of a $CHCl_3$-air atmosphere, when it is kept constant, is in man invariably associated with changes in the condition of the muscles and in the size of the pupil, as also with alterations in the state of the blood, and in the frequency of respiration. These changes remain stable for a while. But a comparison of records taken at successive intervals shows that, after a period of varying extent, they undergo a variation which is manifested by an addition to the degree of their intensity, and that the variation increases in degree during the continued action of $CHCl_3$. So that the change in the former is directly proportioned to the duration of the latter. The period of stability varies in length with different proportions of $CHCl_3$ in the mixed atmosphere. And a comparison between its extent

and the degree of $CHCl_3$-action shows that they are inversely related—*i.e.*, the greater the degree of $CHCl_3$-action, the shorter is the period of stability. It will be longest, therefore, when the lowest degree of $CHCl_3$-action is used to produce unconsciousness—viz., the anæsthetic degree.

To maintain the same degree of unconsciousness, it is necessary to reduce methodically the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere. From this fact the inference follows that some part or parts undergo a change of condition in the course of $CHCl_3$-action, in the way of opposing less resistance to its influence.

The consideration of these facts, which are obtained not from one period of the degree of $CHCl_3$-action only, and that oftentimes the most favourable, but from a comprehensive study of all the stages of different degrees of its action, leads to the isolation of a datum which intermediates between them and the conclusion—viz., the nature of the physiological action of $CHCl_3$. This datum is contained in the following proposition. The phenomena which invariably accompany the action of $CHCl_3$ tend to undergo an increase in the degree of their intensity during its course.

In order to obtain pure $CHCl_3$-results, it

is requisite to exclude the action of a dependent collateral cause—viz., mechanical obstruction. For muscle-relaxation is one of the concomitants of $CHCl_3$-action, and under favourable circumstances the base of the tongue is displaced backwards, thus obstructing, in less or greater degree, the air-way. And in order to obtain pure physiological results, it is requisite to exclude its undue physical action. This is attained by regularity in its administration—*i.e.*, the $CHCl_3$-air atmosphere is kept constant. But if it be proposed to increase the proportion of $CHCl_3$, so as to determine the changes following upon the higher degree of its action, its physical attribute necessitates the gradual introduction of the increment. For if it be made abruptly, an interval will elapse before the respiratory machine accommodates itself to the change in its surroundings—viz., the presence of an excess of $CHCl_3$-vapour in the air-way. And erroneous inferences may be drawn from the phenomena which appear during this interval.

The results of a temporary respiratory overdose are twofold. It opposes an undue resistance to the expiratory movements, thus reducing the result of the action of the respiratory machine, the power of which remains unim-

paired. And it prevents free communication between the contents of the alveoli and the external $CHCl_3$-air atmosphere, thus retarding the absorption of $CHCl_3$. But a greater activity of the respiratory machine is needed to move a heavier atmosphere. And the origin of this increased activity is in the altered state of the blood. The blood, however, cannot become sufficiently discoloured without undue impairment of the respiratory machine, unless there is the least possible obstruction in the alveolar circulation—*i.e.*, there is a gradual diminishment of oxygen in the alveoli. A respiratory overdose implies a greater or less degree of rapidity in the decline of the proportion of oxygen in the alveoli. There is consequently a greater or less impediment in the way of the alveolar circulation, and while it lasts the respiratory machine is more or less disabled. But during the interval equilibrium is being effected between the alveolar contents and the external mixed atmosphere, by means of diffusion. The proportion of oxygen in the alveoli increasing, the alveolar circulation is thereby accelerated, and the activity of the respiratory machine is increased in proportion to the effect which the degree of deoxygenation, induced by the change in

the constitution of the atmosphere, exerts upon the respiratory centre. The different spheres of $CHCl_3$-action are thus indicated in the successive stages of a single example. In one, the physical action of $CHCl_3$ is predominant in the air-way, and is associated with diminished frequency and reduced range of the respiratory movements. In the other the action of the respiratory machine is, through the negative action of $CHCl_3$, automatically adjusted to the requirements of an abnormally heavy atmosphere; there is no interference with the absorption of $CHCl_3$, and its physiological relation to the respiratory centre can therefore be properly studied.

The negative action of $CHCl_3$ is inseparably associated with the physiological. But it may be reduced to a minimum, and is so reduced when the degree of $CHCl_3$-action is limited to the anæsthetic. In the higher or narcotic degrees of action, the results of negative action —viz., defective aeration and distension of the pulmonic artery—are to be taken into consideration in investigating purely physiological action. For, unless the negative are differentiated from the positive results, it may chance that the tendencies of the former are erroneously connected with physiological action.

The study of the purely physiological action of $CHCl_3$ is thus involved in intrinsic difficulties, originating in the different spheres of its influence. A respiratory overdose will, if sufficiently intense, prevent respiratory movements. Respiratory arrest, thus physically produced, may be referred to depression of the respiratory centre. The negative action of $CHCl_3$ may be sufficient to cause a moderate degree of distension of the pulmonic artery, and this will be followed by signs of respiratory exhaustion, if continued for an unduly long period. In these circumstances, arrest of respiratory movements will occur at a late stage in the course of $CHCl_3$-action, instead of at an earlier one, as may be the case when a respiratory overdose is the cause. If depression of the respiratory centre be again assumed to be the cause, and $CHCl_3$ the direct agent, it will be necessary to explain why, in one instance a longer, and in another a shorter, interval elapses before the same effect is produced on the same centre. In the course of $CHCl_3$-action, mechanical obstruction may occur in the air-way, and it may undergo a gradual increase of degree, so that in some complexions no abrupt discoloration appears. The continued action of the same degree of action will be

followed by respiratory arrest. If the circumstances in which it takes place are not fully inquired into, the inference may be drawn that the same degree of $CHCl_3$-action has at different times different effects on the respiratory centre. And this is true, but not in the sense intended—viz., that the same degree of $CHCl_3$-action stimulates the centre at one time and depresses it at another. For in the course of the same degree of $CHCl_3$-action the frequency of respiration, which is dependent on the condition of the respiratory centre, progressively increases. All stimulation is followed by its corresponding degree of exhaustion, but as the result of performing more than the normal amount of work, the respiratory muscles tend to become exhausted. It does not necessarily follow that the respiratory centre is depressed or paralysed because the respiratory muscles are temporarily exhausted. The evidence, however, may show that these muscles are as yet not in a condition of exhaustion, though they have been overworked. If arrest of the action of the respiratory machine occurs during the period of its increased activity, it is obviously requisite to adduce proof in support of the following propositions: 1, that the respiratory centre is in a condition of disturbance; and 2, that the nature

of this disturbance is that of depression or paralysis. For it is possible that the centre may be disturbed and yet not depressed nor paralysed.

But it is conceivable that by reason of the complex character of the organism upon which $CHCl_3$ acts, and of the complications that may be consequential upon surgical operations, circumstances may arise and involve the action of a cause which is independent of $CHCl_3$. Thus a change of position may be followed by an undue displacement of the base of an abnormally large tongue; the function of the stomach, if not in abeyance, may be rendered abnormal by an alteration in one of the conditions which affect it—viz., the state of the blood; the sympathetic nerve may be stimulated; or there may be actual loss of blood, which may be rapid or gradual. If we compare, in general, the frequency of occurrence of respiratory arrest in examples to-day with those of former times, a remarkable diminution is apparent, and is due, in large extent, to the better preparation of the patient. But it may still occur in cases of accident or those diseases which affect the economy of the stomach—*e.g.*, intestinal obstruction; and, therefore, it is essential to know its origin, so that its treat-

ment may be conducted on a rational basis. If, again, the comparison be made, not in respect of arrest of respiration but of fall of blood-pressure, the proportion of the latter is found to be largely increased. And this is due to the larger number of surgical operations performed in the abdominal cavity. The change in the incidence of operation consequently increases the probability of the sympathetic nerve being implicated thereby.

These abnormal phenomena, however, do not always accompany the action of $CHCl_3$, because the circumstances which necessitate them are not always present. Thus the sympathetic nerve may be, but is not necessarily, implicated in a surgical operation. And the results of the stimulation of it will be manifested at no definite time, because the incidence of its occurrence is indefinite. The circumstances, then, which characterise their occurrence are the following: first, they are "occasional"; and secondly, indefinite as to point of time.

When a complicatory cause acts simultaneously with $CHCl_3$ their respective results become intermixed, and it is possible that one or more of them may be affected by both causes. It follows, therefore, that analysis is needed in order to separate those which are simple from

those which are complex. In some examples of $CHCl_3$-narcosis, complicated with mechanical obstruction, the dilated pupil is a simple phenomenon, and the indirect result of the narcotic degree of $CHCl_3$-action. But the pupil may in certain circumstances be dilated in simple mechanical obstruction. It is necessary, therefore, to distinguish between the circumstances attending dilatation of the pupil from either of these causes, so that when they concur its exact causation can be determined. The pupil which is not affected in the lower degrees of mechanical obstruction, only becomes dilated on the commencement of disablement of the respiratory machine in the higher degrees of it. And it rapidly dilates to the full while preserving its sensitiveness to the action of light. In $CHCl_3$-narcosis the pupil does not present any definite size, but varies, being larger or smaller according to the greater or less degree of $CHCl_3$-action. It remains constant for an interval, and afterwards begins to increase, the degree of narcotic action being maintained constant, but the rate of its progressive dilatation is gradual. The dilated pupil of $CHCl_3$-narcosis is invariably associated with sluggishness in its reaction to light. It may thence be inferred that the sluggishness of the pupil suffices to

differentiate between the dilatation of $CHCl_3$-narcosis and that of mechanical obstruction. But the inference is only true on the assumption that dilatation is a simple result. For it may be a complex one, and due to a high degree of mechanical obstruction co-operating with the narcotic action of $CHCl_3$. Now in $CHCl_3$-narcosis (excluding the terminal periods) there is impairment of, but no interruption in, the function of the respiratory machine. The absence of disablement of the respiratory machine is thus incontestible evidence against mechanical obstruction as the cause of dilatation.

Respiratory inhibition occurs during the state of normal anæsthesia, complicated with the abnormal action of the stomach. The ordinary relation between $CHCl_3$-action and the respiratory centre is temporarily suspended. It is essential, therefore, to isolate the cause of the inhibited action of the respiratory machine, because the principles of inductive investigation require proof that when a phenomenon occurs during the operation of an agent, the action of which is the subject of inquiry, it is not only not caused by the agent in question, but also that its actual cause shall be demonstrated to be both present and in action at the time of its occurrence. The presence of a cause in

action is inferred from the phenomena which invariably accompany it. When it ceases to act these phenomena begin to disappear; but the rate of rapidity of their disappearance is not the same in the case of all causes. Thus, reflex causes, supposing that the results of their action are not complicated, are followed by a comparatively rapid return to the normal. For example, reflex stimulation of the vaso-motor centre displaces the blood from the main into the portal circulation, consequently the tension of the pulse is reduced, and it may temporarily disappear. The return of the blood to the main system is by way of the alveolar circulation, and necessarily occupies an interval of time, by reason that the respiratory muscles require their normal blood-supply, of which they have been suddenly deprived, before they can normally perform their function. Thus the action of the respiratory machine determines the backward return of the blood—by supplying a relatively sufficient amount of air to the alveoli to continue the function of aeration, which is begun by diffusion when the air-way is normally patent—and is itself determined by the varying condition of the respiratory centre. The practically important result of vaso-motor complication is the displacement of blood into the portal system,

and its return to the main circulation is the rational object for treatment. And the disappearance of the pulse is thus perceived to be an accidental phenomenon, resulting from the displacement of the blood. In the case of functional arrest of the activity of the respiratory centre, there is a fall of blood-pressure, and the complexion becomes pallid. During the brief period of its arrested action the complexion undergoes a change of colour and becomes livid. But after it is released it immediately resumes its normal action, and consequently the natural colour of the complexion is very quickly restored, the interval between the resumption of spontaneous respiration and the appearance of the natural colour of the complexion being less than 10″, whereas that which elapses between the sudden disappearance of the pulse in the severer examples of vaso-motor complication and its return to the normal amounts to 55″. And this difference leads to the inference that the vaso-motor centre more readily recovers from secondary than primary reflex disturbance.

As compared with reflex causes, mechanical obstruction, and the action of those agents which exert a direct influence on nerve-centres, require a longer time for the disappearance of their results after they cease to act. For example, the

subcutaneous injection of strychnia is followed by convulsion, which is the manifestation of a particular abnormal condition of the spinal centres. After its disappearance many hours elapse before these centres are able to actuate the muscles normally. But in the case of mechanical obstruction, distinction is to be made in regard to the different periods of its duration. For one of its indirect results is distension of the pulmonic artery (physiological pulmonic congestion), and the longer it endures the longer time is required for its complete disappearance. And the reason is this. The effect of mechanical obstruction, which is the ultimate cause, is a diminution of the normal supply of air to the alveoli,—consequently, the alveolar circulation is obstructed. If, therefore, mechanical obstruction is continued, its effect is—not upon a normal condition of the alveolar circulation, as when it first commenced to act, but—upon an obstructed alveolar circulation. An alteration is induced in the condition of the part which is primarily affected. It does not remain constant, but undergoes a further increase of degree during the action of the cause. Thus its direct result undergoes an increase of degree. If, now, this result becomes a cause, as it does in the case of pulmonic congestion, its result—viz., venous

distension—will be increased in degree as the remote consequence of the continued action of its ultimate cause. When, therefore, the latter is put out of action, venous distension does not immediately and completely disappear, but it begins to undergo a diminution of its degree. It completely disappears when its proximate cause, pulmonic congestion, is removed by the continued supply of the normal amount of air to the alveoli.

1. The dilated pupil of $CHCl_3$-narcosis complicated with mechanical obstruction in a moderate degree; and 2, respiratory inhibition occurring during $CHCl_3$-anæsthesia, are simple phenomena associated with the simultaneous actions of two agents. But it is conceivable, and therefore possible, that both causes may affect either directly or indirectly the same part. The phenomenon or phenomena, resulting from the multiple disturbance produced in the common part, will thus be complex, and capable of being separated into their components. Thus, in the intermixture of results derived from the actions of two or more agents operating simultaneously, two different classes of phenomena may exist, the simple and the complex. And consequently it becomes requisite to differentiate the simple results of one cause from

those of the other, and in the case of complex results to analyse these into their components, so that the part which each cause plays in their production shall be properly defined. For two causes in simultaneous operation may act either concurrently or in opposition to each other. Thus, mechanical obstruction and the negative and physiological actions of $CHCl_3$ are all associated with increased frequency of respiration, while the narcotic action of $CHCl_3$ and mechanical obstruction are both associated with discoloration of the blood. On the other hand, in functional arrest of the respiratory centre, circumstances may intervene dependent upon one or other of the different actions of $CHCl_3$, and render the arrested action of the respiratory machine, which is naturally restricted to certain limits of time, relatively permanent. In such a contingency there will be evidence of disturbance in the respiratory centre, and it may, unless analyses of all the circumstances be made, erroneously be referred to the direct action of $CHCl_3$.

In reflex stimulation of the vaso-motor centre the main mass of the blood is diverted into the portal system. Its return to the general, is through the alveolar, circulation. But this may be obstructed as the consequence either

of the negative or physical action of $CHCl_3$ or of mechanical obstruction. Thus, a fall of blood-pressure which in normal circumstances is of transitory duration, will in one or another or a combination of these abnormal circumstances become relatively permanent during their existence, and this induced prolongation of its duration may lead to the inference that the heart has ceased to functionate, but erroneously. For the fact is that there is an interval between the reduced action of the heart and its cessation, during which it is in the most unfavourable conditions endeavouring to overcome an obstacle opposing a greater or less resistance to the performance of its function. This endeavour is manifested by the increasing distension of the veins. The application of cardiac stimulants, based upon a mistaken notion that the heart is directly weakened by the action of $CHCl_3$, is not, therefore, and cannot be in these circumstances, of any avail. What is requisite is the removal, as quickly as possible, of alveolar obstruction. For this is the cause which prevents the recovery of the normal function of the heart from a condition of natural depression, the indirect consequence of vaso-motor stimulation. Alveolar obstruction is the direct result of the negative

influence of $CHCl_3$ in the higher degrees of its action. Its tendency is to diminish the frequency and increase the strength of the cardiac heat. In uncomplicated examples of $CHCl_3$-narcosis this tendency is partially counteracted, and it is accompanied with a diminution of the normal amount of blood in the main circulation. The diminution, however, is effected mechanically and gradually through the distension of the general venous system, not reflexly and suddenly. But in $CHCl_3$-narcosis, complicated with reflex fall of blood-pressure, though the obstacle—viz., the less or greater degree of alveolar obstruction—remains of the same intensity, yet the power of the heart is temporarily reduced. And thus in the new set of conditions affecting the main vascular system, the degree of intensity of the obstacle becomes relatively increased, and therefore opposes a greater degree of resistance to the natural recovery of the cardiac function.

Thus, arrest of respiratory movements and failure of the heart's action may both be complex results. And when such is the case it is requisite to analyse each into its simple components, and to ascribe the latter to their proper causes.

But these results, viz., respiratory arrest and

cardiac syncope, may also be simple—*i.e.*, the product of a simple cause which is independent of $CHCl_3$-action, though acting simultaneously with it. In the case of the arrest of respiratory movements, this cause is complete mechanical obstruction, and in that of cardiac failure, it is inherent in the heart itself (primary cardiac syncope).

Again, both these results may be simple and deriving from causes which are dependent on the action of $CHCl_3$. For example, an excess of $CHCl_3$-vapour in the air-way causes arrest of the movements of respiration; and exhaustion of the respiratory muscles and cardiac exhaustion, the indirect results of $CHCl_3$-action, are the natural terminations of the state of $CHCl_3$-narcosis.

Thus, when different causes may operate at different times to produce the same result, it becomes obviously requisite to recognise each of them by the set of phenomena which invariably accompanies it. The first of these phenomena to appear is called the fundamental phenomenon, because it points to the cause. But, by reason of the rapidity of succession of the phenomena, which is prominent in reflex causation, the possibility arises of mistaking a secondary for the fundamental phenomenon. In

these circumstances the isolation of the cause is to be effected not by means of a single phenomenon, but of all the phenomena which are present, because the selected phenomenon may be common to two or more different causes. From this fact it follows that a greater or less degree of resemblance exists between different states, according to the number of phenomena which they possess in common. Knowledge of the differentiating phenomenon is therefore essential in order to distinguish between two resembling states which might otherwise be taken to be identical. For the results of different causes, though they appear to be alike, are not in all respects exactly similar.

When two or more causes are acting simultaneously, as may happen during the action of $CHCl_3$, and all of them vary in degree of intensity, it is impossible, on the supposition that the nature of their respective action is unknown, to know how much of the results are due to one and how much to another. In order to this it is necessary to limit the action of one to known results, so as to be able to determine what changes occur in any of them, and what new ones appear when the other comes into action. Now, the degree of $CHCl_3$-action is capable of being limited, and the set of phe-

nomena or state associated with it maintained constant by the administration of a constant $CHCl_3$-air atmosphere. A difficulty, however, arises in the fact that the state thus induced is only constant for a period, but it is overcome by progressively diminishing at certain intervals the proportion of $CHCl_3$. By this means constancy is attained with regard to three results—viz., the colour of the blood, the condition of the cerebral centres, and the size of the pupil. The accelerated respiration and increased frequency of the pulse which are associated with $CHCl_3$-action do not remain constant, but exhibit a tendency to increase while the degree of $CHCl_3$-action is in course of being reduced, but the rate of increase in both respiratory and cardiac frequency is definite. For example, the pulse-frequency during the course of normal $CHCl_3$-anæsthesia is found to be 110. The time at which this acceleration occurs is, relatively to the duration of anæsthesia, 45′ from its induction. But the normal increase reaches at this stage to 80. There are, therefore, two causal factors affecting the frequency of the pulse. And the difference between its actual frequency and what it would be if no complicatory cause intervened represents the degree of action of the latter.

After an interval, which is greater or less according to the duration of the complicatory cause, the frequency of the pulse returns to the normal for the stage in which it is taken.

Under normal conditions the action of $CHCl_3$ limited to the anæsthetic degree is associated, 10′ after its induction, with a pulse-frequency of 73. At this stage mechanical obstruction, *i.e.*, backward displacement of the base of the tongue, may naturally intervene (or be artificially produced), and cause a reduction of this frequency to 60. The difference is the measure of the amount of mechanical obstruction present. If the degree of obstruction is increased, the reduction of pulse-frequency is also increased, in accordance with the law that the amount of result is proportionate to the quantity of the cause. But in the case of some tissues the results of low degrees of action of particular causes are not immediately manifested, nor do they appear until after the lapse of an interval, by reason of their power of accommodating themselves within certain limits to changes in their surrounding conditions induced by these causes. Thus, muscle-tissue is not so sensitive to the deprivation of oxygen as is the respiratory centre. For a slight diminution of the normal amount of oxygen in the blood is immediately

followed by a corresponding degree of stimulation of the latter, as is manifested by the increased frequency of respiration, while the same degree of deoxygenation is associated with no change in the condition of the former for a comparatively long interval. Further, the degree of deoxygenation may be so low as not to be associated with any apparent alteration in the colour of the blood. It is known that as the degree of deoxygenation, outside this limit, tends to be increased, so does the degree of discoloration tend also to be increased. It may be inferred, therefore, that the abstraction of oxygen within this limit does not interfere with the condition upon which the normal colour of the blood depends.

$CHCl_3$ is like any other cause, in that it has and can have but one effect. If more than one effect is present, the rational inference is not that $CHCl_3$ itself causes these effects, which is contrary to the laws of causation, but that it is associated with the action of one or more agents—*i.e.*, $CHCl_3$ which is assumed to be pure is actually impure. Such impurity may arise from decomposition, for it is known that $CHCl_3$ is an unstable compound.

What, then, is this effect? The first phenomenon to appear in the course of the adminis-

tration of $CHCl_3$ is acceleration of the respiration. And this points to the respiratory centre as being the part affected. It might, therefore, be inferred that $CHCl_3$ stimulates the respiratory centre. But stimulation of this centre may conceivably be caused either directly or indirectly. Now the former supposition requires that $CHCl_3$ shall be absorbed into the blood, circulate in it, and be conveyed to the centre. But the existence of $CHCl_3$ in the blood of the main circulation is not proved.

There is, however, another difficulty which appears at the threshold of the investigation. $CHCl_3$ cannot be administered by means of the act of respiration without the displacement of air. The diminishment of oxygen in the $CHCl_3$-air atmosphere which is respired, is followed by a corresponding degree of deoxygenation of the blood; and deoxygenation of the blood is invariably associated with stimulation of the respiratory centre. The negative action of $CHCl_3$ thus intervenes and frustrates the inquiry. For, as the proportion of $CHCl_3$ is made to vary, so does that of air also vary. And the variations of respiratory frequency which accompany changes in the constitution of the $CHCl_3$-air atmosphere are associated with two causal factors—*viz.*, the displacement of air

through the negative action of $CHCl_3$, and the physiological action of the latter. If we take the discoloration of the blood, we find this negative action still obstructing the inquiry. For the degree of discoloration increases in direct proportion to the increase of the $CHCl_3$-constituent, but, at the same time, the amount of air is correlatively diminished. The negative action of $CHCl_3$ is thus an important factor in the solution of the problem; and it is requisite to determine what proportion of any given result is due to its influence.

The condition of the part which is primarily affected by the cause is one of the determinants of the result. It may be normal or abnormal. If normal, its quantity has to be taken into consideration; if abnormal, in addition to quantity, both the kind and the degree of abnormality have to be isolated. For example, the same amount of pigment will produce different degrees of tints when dissolved in different quantities of its solvent. And different quantities of weight will produce different degrees of impression upon the same substance, which thus opposes a greater or less degree of resistance to the agent affecting it. It is obvious, therefore, that unless, on the one hand, analysis is made of the quantity of the

part affected and the degree of resistance which it presents, and, on the other, of the different degrees of action of the agent, misconception will arise respecting the actual influence of the latter. And this applies in particular to the case of $CHCl_3$ as the agent. Thus, the same amount of $CHCl_3$ is associated in some instances with a low, in others with a high, degree of results. The inference is not that the same quantity of $CHCl_3$ causes by itself different results, but that the effect of the same quantity of $CHCl_3$, which is necessarily always the same, is modified by differences in the condition of the parts on which it acts. Now it may be that some of the parts, which are assumed to be directly affected, do not present any variation of their initial condition, or at least such a degree of variation as to be of practical importance. Such is the fact in respect of the respiratory centre, and ordinarily in that of the spinal centres. Hence, the initial condition of those centres is regarded as constant; and when any agent exerts a direct influence upon them, the result is wholly ascribed to its action. But the initial condition of other parts which are directly affected may be a variant. And it is in this contingency that it is requisite to give proper allowance to the

variation of condition. For the results occurring during the action of an agent upon a part, the condition of which is not constant, are not wholly due to the agent. And in the case of $CHCl_3$-action, one of the sources of perplexity is removed when the result is differentiated into its factors—viz., the effect of $CHCl_3$ and the influence of the part affected. For the error is thereby avoided of mistaking the $CHCl_3$-result, which is complex, for the effect of $CHCl_3$ which is simple.

But the initial condition of the part directly affected, whatever it is, may not continue constant, but undergo variations in the progress of the action of an agent. Such are the consequences of nutritional interference, which, by lowering the vitality of tissues, diminishes their power of resisting the influence of an agent that is antagonistic to them. The consideration of this possibility during the continued action of $CHCl_3$ leads to the removal of another source of perplexity. For it will appear that while the degree of $CHCl_3$-action remains constant, the results, which are directly or indirectly associated with it, vary.

The effect of $CHCl_3$, which is observed by its negative action, remains, therefore, to be isolated by means of Inductive Investigation,

which consists of two methods—the Method of Agreement and that of Difference.

In the Method of Agreement, the degree of $CHCl_3$-action is constant, while the conditions of the parts which are within the sphere of its influence vary. But, seeing the intimate relation that exists between $CHCl_3$ as a heavy vapour and the action of the respiratory machine, it is necessary to exclude its undue physical action in all experiments relating to its physiological action. It is assumed, therefore, that the administration of $CHCl_3$ is so conducted as not to interfere unduly with the action of the respiratory machine. And it is also necessary to include all the results, for it is possible that if one or more be left out they may be of fundamental importance.

The collation of the records thus obtained show differences in the degree of respiratory frequency, in the frequency and character of the pulse, in the size of the pupil, in the colour of the blood, and in the degree of diminishment of muscle-tone. In some—viz., powerful adults—the amount was unequal to produce unconsciousness; in others—viz., healthy children, and adults suffering from anæmia—it was associated with various degrees of unconsciousness. In the former the colour of the blood

is remarked as not showing any perceptible change, while in the latter different degrees of discoloration are noted. Thus the same amount of $CHCl_3$ is associated with no discoloration of the blood, and with different degrees of its discoloration in different examples. The cubic capacity of the air-way is different in children and adults. And the $CHCl_3$-air atmosphere being the same in both, the relatively greater displacement of air in the former is a factor in the causation of discoloration. For the isolation of one cause does not necessarily exclude the presence and operancy of another producing the same effect, though in a different manner. But the difficulty provided by the displacement of air is removed by restricting the comparison to the results which are obtained in examples of equal respiratory capacity. The displacement of air, then, being the same, and the following conditions being assumed—viz., normal structure of the lungs and normal patency of the air-way—it is found that difference in the degree of discoloration still remains,—a fact which proves that displacement of air is not the sole factor in its causation,—and that it is invariably less in degree when the blood is normal, and in some instances it is inappreciable; and invariably

greater in degree when the blood is abnormal. Accompanying the discoloration of the blood, there are variations of the size of the pupil in the degree of respiratory frequency, in the degree of pulse-frequency, and in that of diminishment of muscle-tone. And these several variations are observed to be not only directly proportioned to each other, but also to the degree of discoloration of the blood. It is inferred, therefore, that a relation exists between the action of $CHCl_3$ and the blood. And, seeing that no nearer relation can be shown to exist between $CHCl_3$-action and either the respiratory centre or the muscular system than that which exists between it and the blood, the inferential proposition that $CHCl_3$ acts directly on the blood takes the place of a subsidiary conclusion in the solution of the problem of its physiological action.

In the Method of Difference, the condition of the parts which come under the influence of $CHCl_3$-action is the same, but the degree of action of the agent is made to differ in different examples, or in the same example at different times. The actual degree of $CHCl_3$-action being noted, and all the results accompanying it being recorded, a comparison is instituted of different examples, in order to determine

whether there be any difference between a low and high degree of its action, and if there is, to define it. But it is to be observed that in the course of these experiments the introduction of $CHCl_3$ to its maximum proportion in the $CHCl_3$-air atmosphere is to be effected gradually, so as to avoid a temporary respiratory overdose. And the maximum proportion which is made to vary determines the particular degree of $CHCl_3$-action, the physiological results of which are under investigation.

The blood being more or less discoloured in all instances, it is found that while the phenomena remain the same in kind, they present different degrees of intensity which are directly related to each other in different instances; that these variations in the degree of their intensity are associated with variations in the degree of $CHCl_3$-action; and lastly, that variations of the one are directly proportioned to variations of the other. Thus, the set of phenomena being termed the state of narcosis, the lower the degree of $CHCl_3$-action, the lower is the degree of narcosis, and the higher the degree of its action, the higher the degree of narcosis. There is a fact, however, connected with the continued action of any degree of $CHCl_3$ which is apt to be overlooked, but which has an important

bearing upon the nature of its physiological influence. It is this: the results which are associated with the continued administration of a constant $CHCl_3$-air atmosphere do not remain constant, but tend, after an interval of stability, to undergo an increase in their degree. And this interval is found to vary inversely in length according to the degree of $CHCl_3$-action—*i.e.*, the higher the degree the shorter is the interval. But the results are maintained constant by progressively reducing, at given intervals, the degree of $CHCl_3$-action. From this fact the inference is drawn that some part or parts, which are directly or indirectly affected by $CHCl_3$, undergo a change of their condition in the course of its action. And the Law of Diminishing Resistance is founded upon it.

If, now, the action of $CHCl_3$ is reduced to its lowest degree—*i.e.*, associated with the state of unconsciousness which is known by automatic respiration, by progressively diminishing the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere—the following alterations become manifest, viz., the discoloration of the blood is less, and the size of the pupil is smaller. These alterations proceed until the blood reaches its normal colour, and the pupil becomes pin-point. Thus a different set of phe-

nomena accompany the lowest degree of $CHCl_3$-action from that which is associated with the higher or narcotic degree. For whereas in the former, which is called the anæsthetic degree for the purpose of definition, the colour of the blood is normal and the pupil contracted or pin-point, in the latter, the narcotic, the blood is discoloured and the pupil is dilated. And a comparison of these two states leads to the conclusion that different degrees of $CHCl_3$-action are apparently associated with different kinds of results on the blood and the pupil respectively. The anæsthetic degree, however, possesses the same tendency as the narcotic—viz., the results in the course of its action present a progressive increase in their degree, together with the appearance of the phenomena which characterise the state of narcosis. And thus the same degree of $CHCl_3$-action which is anæsthetic at one period comes to be narcotic at a subsequent one.

In order, then, to maintain the set of phenomena which is called the state of anæsthesia, constant, it is necessary to diminish progressively the degree of $CHCl_3$-action—*i.e.*, to reduce the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere at the end of successive intervals, the lengths of which are not equal,

but become greater in accordance with the law already enunciated, as the degree of $CHCl_3$-action is reduced. While, however, constancy is maintained by this means with respect to the normal colour of the blood, the contracted or pin-point pupil, and automatic respiration, it is noted that variations exist of the frequency both of the respiration and the pulse. These variations are traced to initial abnormal conditions of the respiration and the blood, and also to initial cardiac abnormalities. When the conditions of these parts are always normal, and the degree of $CHCl_3$-action limited to the anæsthetic, then the frequencies of the pulse and of respiration are found to be invariably the same over that period of life in which they tend to be constant—viz., between the ages of 25 and 45. The state of normal anæsthesia is thus isolated, and with its maintenance the study of causes which intervene in the course of $CHCl_3$-action can be properly carried out. For a standard is attained to which abnormal phenomena are referred. Thus the degree of $CHCl_3$-action being initially limited and subsequently regulated so as to be of itself invariably associated with the state of normal anæsthesia, at any given moment, the pupil is observed to be dilated.

The dilatation of the pupil is the indication of the action of some cause other than that of the anæsthetic degree of $CHCl_3$-action. The phenomena accompanying the dilated pupil are then recorded, and as these include variations in both the frequency and character of the action of the respiratory machine, and in the frequency of the pulse, and possibly in the colour of the blood, the need of the normal $CHCl_3$-standard of these factors is obvious. Thus the means are obtained which lead to the isolation of the complicatory cause.

But there is yet another fact connected with the continued action of $CHCl_3$ which is of first-rate importance with regard to its physiological influence. The frequency of respiration tends to become increased, and with it the frequency of the pulse. Thus, while the normal colour of the blood and the contracted or pin-point pupil remain constant standards for all the stages of the state of anæsthesia, the frequency of respiration is a varying standard, and is relative to one particular stage. The importance of this fact is seen in this, that a progressive diminution in the degree of $CHCl_3$-action is associated with a progressive increase in the degree of respiratory frequency.

The anæsthetic degree of $CHCl_3$-action is not the same for all individuals, but is determined by the amount and quality of the blood. And as $CHCl_3$ is conveyed to the alveoli, where it is absorbed into the blood through the intermediation of the respiratory machine, it follows that if any abnormality be present in the latter, the corresponding alteration in the method of administration is necessitated. With the exercise of due and proper control over the action of $CHCl_3$ in its twofold relation to the blood and respiratory machine, law and order are introduced into the realm of $CHCl_3$-phenomena.

$CHCl_3$-unconsciousness is associated both with the normal and abnormal colour of the blood, with the normal colour in anæsthesia, and with discoloration in narcosis. And the fact that it is so introduces a formidable difficulty into the problem. For it may be concluded with certainty, that when the blood is discoloured the volume of its oxygen is diminished. But is it proved that oxygen may be abstracted without the blood undergoing any variation of colour? It is necessary to explain, therefore, how it is that $CHCl_3$ as an agent causing unconsciousness is accompanied with different conditions of the blood, as also the manner of causation of the dilated pupil of

narcosis; because no solution of the problem is valid which leaves unexplained any one of the phenomena that belongs to any degree of $CHCl_3$-action.

$CHCl_3$ has three separate spheres of operancy. Its vapour displaces air in the $CHCl_3$-air atmosphere, and consequently less than the normal proportion of oxygen is inspired. This is its negative action. Secondly, by reason of its density it exerts its physical action in the air-way, and opposes resistance against the motor-power of the respiratory machine. This resistance, however, is kept constant by maintaining the same $CHCl_3$-air atmosphere throughout the whole of the air-way. Thirdly, $CHCl_3$ is absorbed into the blood and exercises its physiological influence on the part to which it is causally related. The neglect to differentiate between the results of these several actions leads to erroneous inferences; for it may happen as the consequence of some fault in the method of administration that an excess of $CHCl_3$-vapour is present in the middle air-way in such degree as to prevent the action of the respiratory machine. If, now, the physical action of $CHCl_3$ be ignored, the conclusion appears to be inevitable that the arrested movements of respiration are in some way connected with its

physiological action, and that the only way by which respiratory arrest can be caused by $CHCl_3$ is by its depressant action on the respiratory centre.

But, though physical action may be excluded as not interfering with the investigation of pure physiological results, in the case of moderate degrees of narcosis it is impossible to exclude negative action. For negative action is related both to the condition of the blood and that of the respiratory centre. Inasmuch, therefore, as the negative and physiological actions of $CHCl_3$ are inseparably associated with one another, it follows that their respective results will be intermixed: and hence the necessity arises to distinguish between negative and physiological results. But the possibility is also to be entertained that some of the results are complex—*i.e.*, the same part is affected by both actions, but in different ways.

Negative action varies in degree, and is directly proportioned to the degree of $CHCl_3$-action. One of its results—viz., discoloration of the blood—is counteracted in anæsthesia by the increased frequency of respiration. But in narcosis, though the frequency of respiration is higher than in anæsthesia, the proportion of air displaced in the $CHCl_3$-air atmosphere is

greater, and the natural effort towards the normal oxygenation of the blood in these abnormal conditions affecting aeration becomes unavailing, with the result that the blood is imperfectly oxygenated, and as deoxygenation in these circumstances is invariably associated with discoloration, is discoloured.

Now the degree of negative action being a known quantity, its results are capable of measurement. Thus, a certain degree of discoloration of the blood and of respiratory acceleration on the one side, and a correlative degree of pulmonic congestion on the other, are associated with the displacement of a certain amount of air. And the manifestations of pulmonic congestion—viz., venous distension and the reduced frequency and increased strength of the pulse, both which are causally related to the over-distended right ventricle, as the direct result and intermediate cause—are in regard to their intensity determined by the degree of action of the ultimate cause, provided that no complication intervenes and affects the cardiac function,—a contingency which may appear in the progress of $CHCl_3$-narcosis, and is dependent on circumstances attending surgical operations. Unless, therefore, the actual amount of air displaced is known, and the degree of respiratory

acceleration due to it is determined, the conclusion that the negative action of $CHCl_3$ is the ultimate cause of all the respiratory acceleration cannot be certain, but only probable. The uncertainty arises in the possibility that another cause may be present and produce the same result. On this supposition respiratory acceleration is a complex result, the factors in its causation being the negative and physiological actions of $CHCl_3$. If, then, it is demonstrated that x representing the degree of respiratory acceleration due to negative action, the degree of acceleration associated with the administration of a $CHCl_3$-air atmosphere is $x+y$, it follows that y represents the part of the result which is due to physiological action. And the question next to be solved is, "Does $CHCl_3$ cause stimulation of the respiratory centre directly or indirectly?"

The measurement of the degree of negative results is fundamentally important, because negative action explains many of the phenomena which are consequential upon $CHCl_3$-action. But it does not explain the suspension of the functions of the cerebral centres in anæsthesia, where it is present in insufficient degree to cause unconsciousness, and, therefore, also in narcosis, where, though its degree of action is greater,

it cannot be the predominating factor; and for this reason—simple displacement of air is associated with unconsciousness when the blood is intensely discoloured, and this condition can only be effected by respiratory embarrassment. Now, in narcosis, within given limits of degree and duration, there is no respiratory embarrassment.

A cause of unconsciousness being present, but its degree of action proved to be insufficient, provides a reason for the direct action of $CHCl_3$ on the cerebral centres. Against this assumption, however, the following objections are adduced. The recovery of their functions, after being suspended by $CHCl_3$-action, is relatively quick as compared with the longer time which elapses between unconsciousness produced by some other agents—*e.g.*, morphia, and the return of complete consciousness—a comparison leading to the inference that the actual condition of the cerebral centres is different in these examples, and that the result of morphia upon them lasts for a longer time than that of $CHCl_3$. Thus, the latter may be said to be evanescent so far as its action on them is concerned, while that of the former is relatively permanent. But there are difficulties standing in the way of this

view which require explanation. First, the cerebral centres can become habituated to the use of morphia, so that an increasing degree of its action is requisite to produce the same degree of result on them; and secondly, the action of morphia may be different from what it is assumed to be—*i.e.*, it may be progressive, not instantaneous. On the other hand, some agents causing unconsciousness appear to be allied to $CHCl_3$ in the manner of their action: such are chloral, alcohol, and bromide of potassium. It is possible that all these may have a common mode of action. And it is conceivable that there is but one mode of action by which the suspension of the functions of the cerebral centres can be effected.

Another objection to the assumption that $CHCl_3$ directly affects the cerebral centres, appears in the occurrence of the dilated pupil in narcosis. There is no direct relation between the size of the pupil and the state of unconsciousness. The pupil is contracted in anæsthesia, and the iris is sensitive; while the degree of dilatation varies in narcosis, and the iris presents correlative degrees of insensitiveness. Now, the causation of the dilated pupil cannot be ascribed to negative action. For simple displacement of air is not causally as-

sociated with dilatation of the pupil, except in the circumstances of intense discoloration of the blood and embarrassment of the action of the respiratory machine. Besides, when it is so dilated, it invariably preserves its sensitiveness. These two results—viz., unconsciousness and the dilated pupil—stand out as the characteristic phenomena of the physiological action of $CHCl_2$. And the evidence (to be adduced later) will prove that they are indirectly related to it.

Inductive investigation applied to the phenomena which appear in the course of $CHCl_3$-action, in the circumstances in which it is ordinarily used, leads, in the first place, to the separation of non-$CHCl_3$ from $CHCl_3$-products. In this procedure, which is effected by rendering the results of $CHCl_3$-action constant, th several causes of the former are isolated These are, 1, mechanical obstruction in the air-way; 2, stomachic inhibition of the respiratory centre; 3, its functional arrest; 4, reflex stimulation of the vaso-motor centre; and 5, primary cardiac syncope. The results of all these causes, except the last, disappear when they cease to operate during the continued anæsthetic degree of action, in favourable circumstances, of $CHCl_3$. And when the

circumstances are such as to necessitate the temporary withdrawal of $CHCl_3$, it is afterwards resumed without their subsequent reappearance (with the exception of a very few examples). Thus, they are not invariably associated with the action of $CHCl_3$ when limited to the anæsthetic degree; and when they occur, their cause can either be actually demonstrated to be present, as is the case with mechanical obstruction, the removal of which is followed by the gradual disappearance of its results, or else inferred with certainty in the case of reflex causes. For the sudden and complete production of a direct result is the characteristic feature of reflex action, and does not belong to any other agent which is in the limited field of the present study.

In the second place, inductive investigation leads to the isolation of the facts and data which are concerned in the elucidation of the physiological action of $CHCl_3$. Thus $CHCl_3$ is demonstrated to be intimately connected with the blood, and the law of diminishing resistance is founded on certain changes which are inferred to take place in the condition of the parts directly or indirectly affected by it. These two data, along with the facts recorded above, provide the requisite material for in-

ductive reasoning, the end-object of which is to isolate the part which is directly acted upon by the physiological action of $CHCl_3$. The change of its condition is then ascertained, and, finally, the physiological effect of $CHCl_3$ determined.

The deductive method of investigation is advantageous in cases where all the phenomena cannot be known, or their degree of intensity cannot be accurately measured. A given phenomenon is then selected, which is generally the most prominent, and a relationship tentatively assumed between it and the cause whose action is the subject of inquiry. And a series of experiments is undertaken with the view of proving that the assumed nexus actually exists between the cause and the phenomenon selected. But it may chance that the selected phenomenon is not the fundamental one, or if it is so, that it is not fundamental in all the instances of its occurrence, by reason of the presence and operancy of another cause besides that, the action of which is under investigation. Thus, a fall of blood-pressure is, in certain circumstances, associated with $CHCl_3$-action. And it may be mistaken to be the fundamental result of that action. But it is also the indirect result of stimulation of the vaso-motor centre,

and a secondary result of stomachic inhibition of the respiratory centre. Again, it may chance that the selected phenomenon is not a simple but a complex product. And when two causal factors, producing the same kind of result, are both related to the agent, the one negatively, the other positively, it is obvious that confusion will ensue if the whole of the result is ascribed to only one of them. But a third chance is involved in the deductive process of reasoning in respect of the causal nexus. For there may be no causal relationship between the agent, the action of which is under investigation, and the selected phenomenon (the true cause of which is concealed), or if such exists, it may not be true for all instances. For example, arrest of respiratory movements may occur, in diverse circumstances, in the course of $CHCl_3$-action. Some instances are causally dissociated from it; others are causally related to it. It is not universally true, therefore, that $CHCl_3$ is the cause of respiratory arrest occurring during its action, and, consequently, doubt is entertained regarding the nature of the nexus which is supposed to exist between $CHCl_3$-action and respiratory arrest, and thereby to explain the universality of $CHCl_3$ as its cause. This nexus is defined by the

following proposition: $CHCl_3$ exercises a depressant or paralysing influence on the respiratory centre. But though the action of $CHCl_3$ is causally associated with some forms of respiratory arrest, it does not necessarily follow that the association is through the centre of respiration; for, besides physiological action, there have to be considered both the negative and physical action of $CHCl_3$. Now, physical action cannot be excluded as a cause of respiratory arrest. But it does not explain all instances of it, which are restricted to the agency of $CHCl_3$. Some instances remain, and as in these the influence of negative action may be excluded, it results that physiological action is sometimes associated with the causation of respiratory arrest. The establishment of the association does not, however, immediately lead to the conclusion that the physiological action of $CHCl_3$ on the respiratory centre is direct, for it cannot be assumed, even in this group of instances of respiratory arrest, that because the respiratory machine is inactive, therefore the centre of respiration is in a condition of depression or paralysis. And for this reason, that the association may be indirect, and expressed in the disablement of the respiratory machine, which is induced by an inter-

mediary cause standing between $CHCl_3$-action and respiratory arrest. Indirect causation is, therefore, to be excluded before it can be shown that $CHCl_3$ exerts a direct influence on the respiratory centre. But in this group of instances exhaustion of the respiratory muscles invariably appears. And it is equal to explain the occurrence of respiratory arrest. A possible cause is thus isolated. But we have no means at present of inferring the actual condition of the respiratory centre. The assumption, therefore, still holds good that the respiratory centre is in a condition of depression or paralysis. But it has to be explained why this assumed abnormal condition of the centre invariably coincides with exhaustion of the muscles, for it is to be remembered that the same narcotic degree of $CHCl_3$-action has been operating for some length of time before the onset of respiratory arrest, and that paralysis of the respiratory centre is not necessarily associated with paralysis of the respiratory muscles. Let it be supposed that prolonged stimulation of the respiratory centre is followed by exhaustion, from overwork of the respiratory muscles, can it thence be concluded with certainty that the centre also is in a condition of exhaustion or depression or paralysis?

But the variety of the surroundings in which the selected phenomenon appears provides internal evidence of the presence and operancy of a cause or causes in addition to $CHCl_3$. The set of phenomena accompanying the physiological action of $CHCl_3$ is invariably the same. And the several components of it present different degrees of intensity, all which are correlatively proportioned to the different degrees of physiological action. If, however, $CHCl_3$ exercises this or that specific influence, in circumstances which on some occasions are diametrically opposed, it follows that these circumstances have no influence upon the causation of the result, whether it be the arrest of respiratory movements or the disappearance of the pulse. But the proposition is not proved that $CHCl_3$ does possess the specific action which is assumed for it. And so long as it remains in dispute, the influence of the circumstances which complicate its action cannot be ignored. For it is possible that they may, either wholly or partially, be responsible for the result to be explained, and, therefore, it is necessary to prove that they are not causally connected with it. For example: the disappearance of the pulse may be associated either with pallor (*i.e.*, no general superficial venous distension)

or with lividity, the characteristic phenomenon of which is distension of the superficial veins, which may vary in its degree of intensity. Because venous distension, the proximate cause of which is distension of the right ventricle, and the ultimate cause is distension of the pulmonic artery (physiologic pulmonic congestion), is absent in the former, it cannot be inferred that its presence in the latter association may be ignored as having no causal connection with the result in question. The presumption that it has not is strengthened by the fact that fall of blood-pressure occurs not only when its degree is of great, but also when of moderate, intensity. But, though in the case of moderate degrees of intensity it is allowed that they are not (and cannot be) of themselves causally associated with the disappearance of the pulse, the possibility is not thereby excluded that their cause may not play a minor part in its production. What is admitted of the moderate degrees cannot, however, be extended to the higher ones. For the increased degree of action of their cause—viz., distension of the pulmonic artery—is of itself equal to explain the result. Thus, the consequence of this analysis is to expose the weak point of the hypothesis concerning the physiological action of $CHCl_3$ in

its relationship to the function of the heart. For it is obvious that when the degree of $CHCl_3$-action is at its highest, the mode of onset of cardiac failure, if $CHCl_3$ has the specific influence which is assumed for it, will be different from that which invariably obtains in the case of temporary syncope from exhaustion. The fact that it is not so is an argument that $CHCl_3$ does not possess this specific action in one group of instances of disappearance of the pulse. And the inference naturally follows that it does not exercise it in its lower degrees of action. For the amount of effect is directly proportioned to the degree of action of the cause. And it is inconceivable that a smaller degree of action of any cause can produce what a larger degree of it cannot.

A fundamental error is committed in assuming that all instances of pulse-disappearance are of like value. In order to determine respectively their significance, classification is needed, and then it will be apparent that the disappearance of the pulse is associated with different sets of phenomena. Now the same cause is invariably associated with the same set of phenomena. Different causes, therefore, are present on different occasions, and acting simultaneously with $CHCl_3$ when the pulse disappears. And the

introduction of a cause acting independently of $CHCl_3$ results in the following possibilities: the disappearance of the pulse may be produced either by $CHCl_3$ alone or by an independent cause alone, or by their combination. It is requisite, therefore, to exclude the influence, either wholly or partially, of an independent cause, before we can conclude that $CHCl_3$ is acting alone on the heart on the occasion of the disappearance of the pulse. It is easy to perceive that the direct result of an independent cause may be mistaken for that of $CHCl_3$. And it is partly in this confusion of results that the view that $CHCl_3$ acts directly upon the heart takes its origin. But when the analysis of all the circumstances attending the disappearance of the pulse during $CHCl_3$-action alone is made, it will appear that its result upon the function of the heart is not direct, but indirect; and further, that it is not positive but negative.

The multiple causation of some of the phenomena occurring during its administration, the various spheres of its action, its indirect influence upon tissue-vitality,—all these unite to render the study of $CHCl_3$ and its surroundings more intricate than it is generally conceived to be. Thus, there are intrinsic difficulties connected with the action of $CHCl_3$ itself, and

there are extrinsic ones provided by the results of causes which are independent of it but operate simultaneously with it, sometimes concurrently, at others antagonistically. And the peculiarity which attaches to them is that they are only occasional in their appearance, and indefinite in the time of their occurrence. There are three possible sources from which any phenomenon may arise: it may be causally associated with some or other of the different actions of $CHCl_3$, it may proceed from a cause originating in the patient, or it may be connected with some circumstance which is related to the surgical operation. The isolation of the cause, say, of the arrest of the action of the respiratory machine is to be conducted, therefore, not by means of partial evidence, but all the phenomena which are present at the time of its occurrence are to be included, as well as all the circumstances which are concerned in its production. And thus the inclusion of all facts requires the following analysis. I. The incidence of respiratory arrest is in the period of the induction of unconsciousness. The method of administration is to be noted. The phenomena antecedent to and accompanying respiratory arrest are to be recorded, as well as its mode of onset and the phenomena ap-

pearing subsequently to it. The principal factors are—1, voluntary arrest or inhibition of the action of the respiratory centre; 2, mechanical obstruction; and 3, respiratory overdose. They are severally distinguished by their characteristic phenomena. II. The incidence of respiratory arrest is in the period of the maintenance of unconsciousness. Inasmuch as there are different degrees of $CHCl_3$-unconsciousness, the following subdivisions are requisite—viz., *A*, respiratory arrest occurring during anæsthesia, which is the lowest degree of $CHCl_3$-unconsciousness; and *B*, respiratory arrest occurring during narcosis, which may vary in degree. Further, seeing that narcosis may be of two kinds—viz., simple $CHCl_3$-narcosis or mixed narcosis—the consequence of mechanical obstruction accompanying the narcotic action of $CHCl_3$ and remaining uncounteracted, it is requisite to form it into two groups: *a*, respiratory arrest occurring during simple $CHCl_3$-narcosis; and *b*, respiratory arrest occurring during mixed unconsciousness, in which the $+CO_2$ factor may be predominant. III. The abnormal phenomena which are antecedent to the onset of respiratory arrest. IV. The phenomena which accompany it. V. The mode of its onset. VI. The phenomena which appear subsequently to it.

The two following examples illustrate the necessity for complete and accurate analysis.

In the first, the administration of $CHCl_3$ was conducted on the lines of the normal method, and so that at no time was there any temporary excess of the vapour in the air-way, nor any discoloration of the blood. The succession of phenomena proceeded normally up to the last stage of the period of induction, when, instead of the onset of automatic respiration which was expected to happen, and thus confirm the experience derived from the generality of instances, arrest of the action of the respiratory machine took place. The circumstances, then, in which this unexpected phenomenon appeared were these: its mode of onset was sudden, and its incidence, as regards the act of respiration, was at the end of expiration. There were no abnormal phenomena antecedent to it, nor did any accompany it; for, at the moment of its occurrence the pupil was pin-point, the colour of the complexion natural, and the pulse normal. But these phenomena were manifested immediately after its occurrence—viz., duskiness, distension of the superficial veins, and a diminishment of frequency with increased strength of the pulse. And their degrees of intensity were progressively augmented, and showed that the

relationship between them was one of direct proportion. After an interval spontaneous respiration was resumed, whereupon $CHCl_3$ was continued.

Now the absence of antecedent duskiness proves that both mechanical obstruction and respiratory overdose, which are possible causes of respiratory arrest, were absent. And as arrest of respiration does not invariably accompany $CHCl_3$-action, when limited to the anæsthetic degree, at the stage of induction in which it occurred, and it may be added nor at any other stage of it, it follows that an exceptional cause is to be sought in order that it may explain an exceptional occurrence. Functional arrest of the action of the respiratory centre is invariably associated with arrest of the action of the respiratory machine at the end of a full inspiration (in normal or during its progress in abnormal conditions). There remains, therefore, but one cause—viz., the act of volition. When unconsciousness intervenes during voluntary action, the results of that action do not immediately disappear, but continue for a while. In the present example it is impossible for the will to release the respiratory centre from the condition of the temporary suspension of its function. But in the meanwhile the state of the blood

becomes changed, and the increase of CO_2 or diminishment of oxygen, or both together, eventually determined the return of its functional activity. As voluntary arrest may occur in the normal, so may it in an abnormal state of the respiratory machine. In the former no artificial means of recovery are required, but in the latter they are necessary, for this reason, that though it is not directly related to the cause of its arrested action, yet its abnormal state may hinder the re-oxygenation of the blood from being effected within a given limit of time.

The second example is one of respiratory arrest occurring in the course of normal anæsthesia. The time of its appearance was 15′ after the onset of automatic respiration, but this is not constant for all instances. And the peculiarity which attached to it is that it did not occur in any one of the previous six administrations to which the patient had been subjected. The mode of onset was sudden, and its incidence in the course of inspiration. Accompanying it was pallor, and the fall of blood-pressure was so intense that the pulse was only perceptible. It was immediately followed by general venous distension, and by discoloration of the blood, which slowly issued from the incision-wound. Under these circumstances the

base of the tongue was placed in its normal position and the lower third of the chest compressed. This treatment was almost immediately followed by inspiration, which again became arrested at its termination, when the act of vomiting took place, after which the abnormal phenomena rapidly disappeared. And as soon as the normal state was reached $CHCl_3$ was continued.

The arrest of the action of the respiratory machine at the end of full respiration is characteristic of functional arrest of the activity of the respiratory centre. And the reason why it was temporarily interrupted in the example just described, is that it was prevented by the unduly abnormal state of the atmosphere which was inspired. A sufficing impediment originated in the coincidence of full inspiration with the maximum $CHCl_3$-air atmosphere. Had it occurred 10″ later, when the greater part of the $CHCl_3$ constituent had been absorbed or dissipated, it is probable that no interruption in the performance of a natural function would have ensued.

The parts principally affected by $CHCl_3$, and the different causes which may act simultaneously with it, are—1, the blood; 2, the respiratory system; 3, the circulatory system; and 4, the pupil. If these are represented by letters,

so that the capital stands for the normal and the small letter for the abnormal condition, and the several components of the respiratory and circulatory system treated in the same way,—thus B = the respiratory system = [R.C (respiratory centre) + A.W (air-way) + L (lungs) + M (motor-power)] any abnormal phenomenon that appears can not only be readily presented with its cause or causes, but also with the abnormal phenomena which accompany it, by means of the following equation, in which A is taken to be the blood, B the respiratory system, C the circulatory system = [V.M.C + Ht + P + V] and D the pupil. A given instance of arrest of the action of the respiratory machine is then found to be represented as follows:—

$$\text{R.A} = \frac{\text{a} + \text{b}\,[\text{R.C} + \text{a.w} + \text{l} + \text{m}] + \text{c}\,[\text{V.M.C} + \text{Ht} + \text{p} + \text{v}] + \text{D}}{\text{abn. } CHCl_3 = \text{air-way.}}$$

And the cause being removed by diffusion—*i.e.*, the $CHCl_3$-air atmosphere is temporarily withdrawn, the abnormal phenomena dependent upon it disappear, and the return to the normal is effected—viz.,

$$\text{n.R.M} = \frac{\text{A} + \text{B}\,[\text{R.C} + \text{A.W} + \text{L} + \text{M}] + \text{C}\,[\text{V.M.C} + \text{Ht} + \text{P} + \text{V}] + \text{D}}{\text{n. } CHCl_3.}$$

A second example is represented as follows:—

$$\text{R.A} = \frac{\text{a} + \text{b}[\text{R.C} + \text{A.W} + \text{l} + \text{m}] + \text{C}[\text{V.M.C} + \text{ht} + \text{p} + \text{v}] + \text{d}}{\text{abn. } CHCl_3 = \text{blood-overdose,}} \text{(insensitive)}$$

in which the differentiating phenomenon is the insensitive dilated pupil. Here, the re-oxygenation of the blood can only be effected gradually, and it may require artificial means. These examples show $CHCl_3$ as the physical or physiological cause of respiratory arrest, but the following is characteristic of an agent which is independent of it:—

$$\text{R.A} = \frac{\text{A} + \text{b}\,[\text{r.c} + \text{A.W} + \text{L} + \text{m}] + \text{c}\,[\text{v.m.c} + \text{Ht} + \text{p} + \text{V}] + \text{D}}{\text{n. } CHCl_3\text{; direct abn. stomachic action;}}$$

but this form may be complicated either with simple mechanical obstruction or a respiratory overdose; in the latter contingency, complex

$$\text{R.A} = \frac{\text{a} + \text{b}\,[\text{r.c} + \text{a.w} + \text{L} + \text{m}] + \text{c}\,[\text{v.m.c} + \text{Ht} + \text{p} + \text{v}] + \text{d}}{\text{abn. } CHCl_3\text{; air-way, direct abn. stomachic action,}}$$

where it is requisite to render the condition of the air-way favourable to the completion of the act of vomiting. But in all instances of stimulation of the vaso-motor centre, whether of primary or secondary origin, the position of the base of the tongue, inasmuch as it may be affected by temporary diminution or loss of muscle-tone, which is indirectly consequent upon fall of blood-pressure, has to be considered. For it may completely obstruct the glottis. In order to counteract the dangerous tendency of such displacement, it is necessary, when a fall of blood-pressure occurs, to maintain by artificial

means the natural patency of the air-way until recovery is complete.

It is requisite to extend observation to all the phenomena, and not to limit it to one. A severe fall of blood-pressure is invariably associated with extreme dilatation of the pupil, but it may or may not be accompanied with immediate suspension or rapid decline of the action of the respiratory machine. It cannot, therefore, be concluded that this phenomenon is of the same value on all occasions. But it may be assumed to be so, and the assumption made to form the foundation of an hypothesis. A series of experiments is then devised in order to prove its truth. But though the results of these experiment are or tend to be uniform, yet, when they are compared with all instances of the phenomena, without reference to the circumstances in which it appears, they are found to present not a universal but only a partial agreement. Why is there not universal agreement? Either because, the hypothesis being true, another (but not necessarily the same) cause is present, and produces some results which do not belong to those of the cause in question. And then to explain discrepancies, all that is needed is the isolation of the disturbing cause. Or else the hypo-

thesis is not true. A mistake is made with regard to the actual part which is directly affected by the agent, whose action is under investigation. But if $CHCl_3$ does not produce fall of blood-pressure by a direct influence on the heart, it is possible that it may do so indirectly. And seeing that the same phenomenon may be produced by different causes, it is also possible that $CHCl_3$ may not, in all instances of it, be the ultimate cause of the disappearance of the pulse.

It is admitted that the results of experimental investigation concerning $CHCl_3$-action on the lower animals do not satisfy the experience which is acquired from its administration to man. And the explanation of the antagonism between them is quite simple. The circumstances in which experiments are conducted are not made as similar as they can be to those which may obtain in the ordinary administration of $CHCl_3$. Thus, with different degrees of $CHCl_3$-unconsciousness, different degrees of stimulation are to be applied to different parts of the sympathetic-nerve system in order to demonstrate where, and to what degree, the progress of a natural action is delayed by one of the results of $CHCl_3$-action: the terminals of the vagi are to be stimulated,

so as to induce the condition which is characteristic of the abnormal function of the stomach, and the actual quantity of the blood is to be artificially reduced, in different proportions, in order to determine the degree of variation of the results accompanying the same degree of $CHCl_3$-action in these altered circumstances. Uniform results are only possible when the circumstances attending their causation are exactly alike. When results are not uniform, the want of uniformity derives from some difference or differences in those circumstances which, in the case of $CHCl_3$ as it is ordinarily used, are—1, difference in the degree of its action, and the duration of it; 2, variant condition of the part which is directly affected by it; and 3, the presence of a complicatory cause, which may be either dependent upon or independent of it.

Not the least interesting question regarding $CHCl_3$-action is, How does it produce unconsciousness? Next, after the centre of respiration, the cerebral centres are most jealously protected by Nature from external injury. And it is matter of common knowledge that their functions may be suspended by the action of certain drugs, and yet their condition is not adversely affected thereby. Does Nature exer-

cise similar precautions in their favour against internal attack?

In the case of opium, the rate of absorption is determined by the volume of the gastric circulation, and as this tends to be reduced by its astringent action on mucous membranes, its absorption into the blood is consequently delayed, the actual amount absorbed being progressively diminished by the increasing degree of vascular contraction. But in the subcutaneous injection of morphia there is no such accompanying safeguard, and an overdose is rapidly absorbed.

In the case of those vapours whose action is followed by unconsciousness, the following facts have an important bearing upon the wellbeing of the cerebral centres.

First, when present in a high degree of concentration, fire-damp and such-like gases (and amongst them $CHCl_3$-vapour may be included) tend, on entering the air-way, to compress its contents towards the alveolar region. This salutary result is the consequence of their density, for it permits of the continuity of the alveolar circulation, though under increasingly unfavourable conditions, and thus tends to relieve, in ever so slight degree, the over-distension of the right side of the heart. There is,

therefore, an interval, and it may be sufficiently long for the salvation of life, in which removal from the noxious atmosphere may be effected, and artificial means of restoration applied.

Secondly, when present in a less concentrated degree, and so as, unconsciousness supervening, to allow of the continuous but abnormal action of the respiratory machine, the action of the agent absorbed into the blood upon the cerebral centres is constant, and tends to endanger their vitality. In these circumstances the future wellbeing of the cerebral centres is safeguarded by the intervention of the respiratory machine. For the degree of pulmonic congestion progressively increases, and determines a corresponding reduction of the quantity of the agent absorbed, and consequently a progressive diminution in the degree of its action. And eventually, if aid be not forthcoming, the respiratory muscles, after manifesting signs of exhaustion, fail to perform their function.

Artificial means of restoration, if applied within the prescribed interval after the onset of respiratory arrest from this cause, are followed by recovery. And it will be observed that the return of the function of the respiratory muscles coincides with the normal reoxygenation of the blood; and further, that

the resumption of their function is complete,—a fact which leads to the conclusion that the respiratory centre had, owing to the temporary disability of the respiratory machine, been prevented from manifesting its activity. Following soon after the normal readjustment of the vital functions, consciousness returns and rapidly becomes normal.

The means provided by Nature, in order to defend the cerebral centres from the injurious action of agents which are absorbed into the blood, are thus diverse. All heavy vapours carry with them their own check to absorption; for, the greater the degree of their concentration, the less is the amount absorbed. But it is curious to perceive the particular manner of their employment which characterises the second group. The cerebral centres and the striped muscles are sensitive, in a greater degree than other tissues, to a diminishment of oxygen in the blood. And the former are more so than the latter. As each tissue possesses an initial power of resistance, the inference is possible, if the circumstances are not taken into consideration, that the cerebral centres will be the first to be injuriously affected. And thus, if there were no counteracting means, the possibility arises

that the body might recover its life while the cerebral centres might lose their functions. To oppose this destructive tendency, which is antagonistic to the Plan of Nature, for the reason that the salvation of the body, without the preservation of the means within itself to continue its existence, is purposeless, the respiratory muscles become exhausted from overwork. And as the consequence of their failure to functionate, the cerebral centres are withdrawn from the sphere of a cause which would, if its influence were continued, destroy them, and left in a condition compatible with the ultimate restoration of their functions, always provided that the circumstances are favourable to the successful application of artificial respiration.

It might be supposed that there is no very near relationship between fever and the ultimate sources of unconsciousness which have just been enumerated. But the state of fever presents the following phenomena which establish a parallel with them. First, it is characterised by increased respiratory frequency, which is the result of a shortage of oxygen, consequential upon the combustion of abnormal products contained in the blood. And, incidentally, it may be suggested that the judicious use of an increased proportion of

oxygen appears to be rationally indicated in high temperature, to neutralise the loss which the blood sustains. Secondly, by the abnormal condition of the cerebral centres, which is manifested by the appearance of delirium and unconsciousness. And in these examples also, if life is saved, the subsequent recovery of the functions of the cerebral centres is complete.

The production of unconsciousness being thus associated with agents differing so widely in their nature, leads to the inference that there is a common cause which is intermediate between them and the result. In other words, that all these ultimate causes produce the same direct result—viz., deoxygenation of the blood—and that this result is the intermediate cause of the suspension of the cerebral functions. And if this be true of all agents producing unconsciousness, then one of the fundamental objects of Nature will be demonstrated—viz., the conservation of the cerebral centres in all circumstances that are prejudicial to their wellbeing.

The principal difficulties which surround the $CHCl_3$-problem are the very same with those involving other intricate studies. Clinically, they appear in the simultaneous action with $CHCl_3$ of causes which are independent of it. It, therefore, becomes requisite to differentiate between simple and complex results, and as

the same simple result—*e.g.*, disappearance of the pulse—may be produced by different causes, one of which is $CHCl_3$-action, to refer each instance of it to its actual and not an imaginary cause; and, in the case of a complex result, to analyse it into its components. Physiologically they appear in the assumed direct causation of phenomena, as that $CHCl_3$ acts directly upon the respiratory centre, without excluding the possibility that its action may be indirect, and in the omission of material evidence, which is of paramount importance to the inquiry.

The development of the theme which has just been outlined is comprised in the following heads:—

I. The critical examination of the commonly received $CHCl_3$-hypothesis, leading to the conclusion that the propositions upon which it is founded are not true.

II. The introduction to the study of causation, simple and multiple, illustrated by examples occurring during the administration of $CHCl_3$.

III. The analysis of all the factors, extrinsic and intrinsic, which are concerned in the solution of the $CHCl_3$-problem.

IV. The isolation of the facts and data upon which the theory of the physiological

action of $CHCl_3$ is constructed, and the verification of the conclusion by a series of experiments.

V. Synthesis—*i.e.*, the construction of a method of administration, based upon the known properties of $CHCl_3$, and capable of being adapted both to variations of the conditions of the parts upon which in its different spheres of influence it acts, and to the requirements of causes which are independent of it, but which may intervene in the course of its action and produce a state of complication. And it is self-evident that no method can be fundamentally sound in which the degree of the physiological action of $CHCl_3$ is not restricted to the limit of anæsthesia—*i.e.*, the lowest degree of $CHCl_3$-unconsciousness, both on the induction and during the progress of the state of unconsciousness. The knowledge of the part which is directly affected by the action of $CHCl_3$ is thus of prime importance in its administration.

THE $CHCl_3$-PROBLEM.

INTRODUCTION.

§ 1. *The $CHCl_3$-Hypothesis.*—The physiological action of $CHCl_3$ was originally founded on inferences, drawn from prominent phenomena which occurred in the course of its operation. The phenomena are—1, convulsion; 2, arrest of respiratory movements; and 3, fall in blood-pressure. The inferences are—1, $CHCl_3$ stimulates the special centres; 2, it paralyses the respiratory centre; and 3, it depresses the function of the heart. But there is no definite statement of the manner of causation in the case of cardiac depression. The causal nexus between $CHCl_3$ and the results which happen during its operation was constructed by deductive reasoning. Because arrest of respiratory movements happens during the administration of $CHCl_3$, therefore it is caused by $CHCl_3$. If any objection was

advanced against the validity of this conclusion, the followers of the hypothesis demanded "what cause other than $CHCl_3$ is present, and in operation?" The possibility of another cause acting simultaneously with $CHCl_3$ was not entertained.

A bias, therefore, was introduced into the treatment of phenomena occurring during $CHCl_3$-action. As a result of it, experiments have been devised to prove "how $CHCl_3$ acts upon the nerves, the nervous centres, and the heart." But suppose there is doubt about the relationship between $CHCl_3$ and the nervous centres, arising from the conflict of evidence. It is obvious that all doubt is to be removed from this fundamental relationship if we are to avoid the introduction of error in experimental results. Let us take the occurrence of "convulsion." Bias affirms $CHCl_3$ to be the cause. Experiment demonstrates that $CHCl_3$ stimulates the spinal centres. But $CHCl_3$ may be administered so as to produce unconsciousness without the appearance of convulsion. The rational procedure is then to inquire, "What is the cause of convulsion?" The isolation of the cause is the end-object of inductive investigation.

§ 2. *Caprice of $CHCl_3$.*—The supporters of the hypothesis were confronted with a difficulty at an early period of their deductions. The so-

called convulsion was general in its occurrence, but by no means universal. And for this reason it had been better to have used the simple statement "muscle-phenomena," instead of a term which tends to create a prejudice in favour of its origin in stimulation of the spinal centres. Besides wanting universality of occurrence, however, they did not present uniform characters. But arrest of respiratory movements or of pulse-failure were not so general,—their appearance was only occasional. And just as the "convulsion" was ascribed to the ordinary action of $CHCl_3$, so, whenever pulse-failure or arrest of respiratory movements happened, these were ascribed to its extraordinary action. Now it is illogical to draw a general conclusion from particular instances. The difficulty was met, therefore, by attributing this extraordinary action to caprice. There is a sudden departure from the course of action with which experience makes us familiar. $CHCl_3$ no longer obeys the laws of causation on these occasional instances. It shows caprice—1, by selecting in one case the heart, in another the respiratory centre, as the seat of its deadly influence; and 2, by the irregularity which characterises the point of time of the onset of crises. For these may occur during the period of inducing uncon-

sciousness, and at any stage in the course of its maintenance.

§ 3. *Evidence in favour of the Hypothesis: occurrence of death.*—Crises are very often, but not invariably, followed by death. The fact that recovery does not take place, provides a substantial argument for the soundness of the hypothesis. For it is admitted, in a given case, that the heart does not regain its function. Then what is the cause of its failure? the peculiar action of $CHCl_3$ on the heart.

But how does the hypothesis stand in regard to instances of recovery? The heart is selected by $CHCl_3$ as the object of its occasional display of deadly action. An initial cardiac abnormality is inferred to be favourable to the development of $CHCl_3$-caprice. And the belief is widely spread that $CHCl_3$ is more dangerous in the case of a weak heart than in that of a normal one. If, therefore, $CHCl_3$ is administered in a series of cases of weak hearts, there should be a tendency to a larger proportion of pulse-failures. The fact is, that the proportion is the same, if no discrimination is made between the kinds of cardiac weakness, as that obtaining in the case of normal hearts. But if pulse-failure occur during $CHCl_3$-action, and the heart is known to be initially weak, then the chance of re-

covery according to the hypothesis is nugatory. But the number of recoveries is larger than that of fatalities. In order to explain this diversity in results, it is necessary to enlarge the basis of the hypothesis. When the heart is directly affected, some instances recover, some end fatally. $CHCl_3$ is the only agent which indirectly causes pulse-failure through cardiac depression. To explain the instances of recovery, it is inferred that the degree of depression which $CHCl_3$ exerts is not sufficient to produce permanent failure of the heart. There is the evidence that the heart recovers its function after passing through a minor degree of crisis. On the other hand, if the heart does not recover, there is evidence of the major degree of the deadly action of $CHCl_3$. The occurrence of these different results leads to the notion of the different degrees of depressant action. And the explanation is framed so as to fit in with the evidence.

§ 4. *Pulse-failures not always under like surrounding conditions.*—If this deadly action of $CHCl_3$ on the heart were invariably followed by like conditions of, 1, the respiratory machine; 2, the circulatory system; and 3, the pupil; the hypothesis would then be considerably strengthened. And if it were further demon-

strated that the antecedent conditions both of the respiratory machine and circulatory systems had no disturbing influence, directly or indirectly, on the function of the heart, the hypothesis would be advanced a step nearer to a proved conclusion. But, unfortunately for it, pulse-failure does not invariably occur under like surrounding conditions, nor is it invariably followed by the same changes in the respiratory machine and the pupil. *A*. Failure of the pulse may occur when, I., the complexion is of its natural colour, the respiratory machine is acting efficiently, and the pupil contracted; or, II., when the complexion is dusky, the action of the respiratory machine is abnormal, and the pupil is dilated. In I. there is no evidence of complication of the respiratory machine. In II. there is, and it is manifested by the presence of duskiness, which is a concomitant of physiologic pulmonic congestion. Physiologic pulmonic congestion is related to disturbance in cardiac function, and is confined to distension of the pulmonic artery. The distension begins in the terminals of the artery, and extends along its course until it reaches the right ventricle. Thus the right ventricle becomes distended as the result of impediment in the alveolar circulation, con-

sequential on the shortage of oxygen in the $CHCl_3$ air atmosphere. The degree of distension varies directly as the degree of alveolar obstruction. Under this abnormal condition the heart does more than the normal amount of work.

Two causes, then, are acting simultaneously on the heart. But the supporters of the hypothesis consider only one of them. If the hypothesis be true, then the condition of the heart at the moment of pulse-failure is not simple, but complex. There is, 1, the result of pulmonic congestion; and 2, the result of $CHCl_3$-caprice. It is necessary, therefore, to exclude the influence of pulmonic congestion before we ascribe the whole result to $CHCl_3$. Now, pulmonic congestion may act in two ways: It reaches a high degree in a comparatively short space of time, or, it is maintained at a moderate degree of intensity, constantly impeding the cardiac function. The length of time during which a moderate degree of pulmonic congestion is acting, becomes an important factor in the solution of the causation of cardiac failure. But pulse-failure occurs without the presence of pulmonic congestion. To avoid the confusion which arises from the tendency towards ascribing to the action of

$CHCl_3$ the result of other causes, it is necessary to record the exact surrounding conditions under which pulse-failure occurs.

B. After pulse-failure there may be, I., no initial interference with the action of the respiratory machine, but the pupil is fully dilated. The action of the respiratory machine gradually declines until it ceases; the pupil remains dilated. There is no return of the pulse. II., There is rapid decline in the action of the respiratory machine immediately following failure of the pulse, and the pupil dilates. If the air-way is rendered normally patent, the pupil rapidly contracts, there is a gradual return to the normal action of the respiratory machine, followed by the return of the pulse. Now, on the supposition that $CHCl_3$ acts directly upon the heart, it matters little whether the condition of the right ventricle is normal or abnormal. The analysis of the antecedent conditions leading up to crisis is, therefore, according to the hypothesis, of no avail. But if differences in conditions at the onset of crisis do not affect its validity, differences in the phenomena consequent upon a sudden failure of the heart will. For primary cardiac syncope, the condition assumed to be induced by $CHCl_3$, is followed by one set of phenomena.

But a different set of phenomena follow upon some instances of pulse-failure, and, if the hypothesis be universally applied, the disappearance of the pulse is produced by the deadly action of $CHCl_3$. The same cause—viz., primary cardiac syncope—is followed by different results, which is contrary to one of the laws of causation.

But it may be objected that these two groups of examples of pulse-failure present different degrees of the sudden and deadly action of $CHCl_3$. How does the hypothesis, then, explain, 1, the non-interference with the action of the respiratory machine in the fatal case; and 2, the rapid decline of it to a minimum in the case of recovery?

§ 5. *The argument against the Hypothesis.*—This is composed of two parts. First, there is the commission of a logical fallacy. Secondly, there is, 1, the omission of certain data which enter into the solution of the $CHCl_3$-problem; and 2, the imperfect treatment of the data which are selected by the supporters of the hypothesis as the basis of deductive inference.

§ 6. *The Logical Fallacy.*—Pallor is one of the concomitants of fall of blood-pressure. Its degree varies, and variations of its degree may be taken as the measure of the degree of the fall

of blood-pressure. Pallor may occur during the course of $CHCl_3$ action. It does not, therefore, necessarily follow that it is an indirect result of $CHCl_3$-action—*i.e.*, $CHCl_3$ acts directly upon the heart so as to depress its vigour and lead to a corresponding fall of blood-pressure. For it is possible that a direct result of $CHCl_3$-action may become an intermediate cause, exerting a direct influence on the cardiac function. And then pallor would be related to the action of $CHCl_3$, not directly, but indirectly, through the heart. But there is another possibility. And it is this. Pallor may not be causally related to $CHCl_3$-action. It occurs during the administration of $CHCl_3$, but it is not caused by it. There is a cause of pallor independent of the action of $CHCl_3$, but acting simultaneously with it.

When there is no demonstrative proof of causal relationship between $CHCl_3$-action and a phenomenon appearing in the course of its administration, the rational position to take up is this: the action of $CHCl_3$ is associated with the occurrence of pallor (or any other phenomenon, for several phenomena occur, at different times, in different cases). The determination of the nature of this association is left to the inductive method of investigation,

and this is composed of three stages. The first is the collection of a sufficient number of cases in which pallor appears, with the accurate and complete description of all the phenomena preceding, accompanying, and following upon it. The second stage is concerned with the classification of the records into groups. And the third deals with the isolation of the fundamental phenomenon. Now pallor may or may not be fundamental. Suppose that it is taken to be fundamental when it is only of secondary importance, the fallacy is committed of deriving the wrong cause. And thus, when there are two or more possible causes of pallor occurring during $CHCl_3$-administration, confusion is introduced by the hypothesis in the inquiry.

But there is another method—the deductive—of investigating the causation of phenomena. It is invariably associated with bias in favour of a particular cause. It was followed by the founders of the $CHCl_3$-hypothesis. Certain phenomena were selected in order to unfold the physiological action of $CHCl_3$. Of these, pallor (*i.e.*, fall of blood-pressure) is one. The question then arises, "How does $CHCl_3$ cause pallor?" But before this can be answered, the question that precedes it needs a convincing answer, "What is the proximate cause of

pallor?" This is assumed to the cardiac depression. Now, as there is on assumption only one cause in operation affecting the heart, viz., $CHCl_3$, it follows without, apparently, the possibility of doubt that $CHCl_3$ depresses the action of the heart. Pallor appears; it is the result of cardiac depression, which is caused by $CHCl_3$. The explanation of pallor is in an assumed condition of the heart. $CHCl_3$ acts directly upon the heart in the way of depressing its function. What is the evidence of this condition of cardiac depression?—the presence of pallor. But this is the weakest form of argument, for it is arguing in a circle. There can be no question of, 1, $CHCl_3$-action; and 2, the presence of pallor. But there may be of the third fact in the argument—viz., the condition of the heart. Now there is no proof of its actual condition. It is, however, assumed to be depressed in order to explain how $CHCl_3$ causes pallor. The proposition that $CHCl_3$ directly depresses cardiac function, is therefore a weak link in the chain of argument. But it is not the only one. For pallor is not invariably the result of cardiac syncope. When it occurs during $CHCl_3$-administration, it is, in the vast majority of cases, the result of reflex stimulation of the vaso-motor centre.

The assumed relationship between $CHCl_3$-action and an assumed condition of the heart has reacted as a barrier in the investigation of natural causation. For it appears to be so near the truth that it is practically taken for it. The same method of reasoning is applied to respiratory and muscular phenomena. The tendency to explain all phenomena appearing in the course of $CHCl_3$-action as the results of it, became widely prevalent. Many modes of procedure were devised for this action. If arrest of respiratory movements occurs, the mode of operation is through the respiratory centre which is paralysed, and the inference is made without regard to the known physiological truth, that the respiratory centre is relatively indestructible. But what are the signs of paralysis of this centre? The superficial thinker might take this question to be completely and accurately answered by "what else but arrest of respiratory movements!" But there are different modes of arrest of respiratory movements. There is sudden arrest during or at the end of inspiration. And there is rapid arrest with or without obstructed respiration. Paralysis of the respiratory centre cannot be followed by all of these modes. Which is the mode belonging to it?

$CHCl_3$ is assumed to depress the function of the heart. The mode of procedure is either through, 1, paralysis of the cardiac muscle; or 2, paralysis of the local nervous centres. Which of these does $CHCl_3$ effect? This part of the problem remains in a state of uncertainty, by reason of the lack of a datum which would relate $CHCl_3$-action either to the muscle or the nervous centres. But a test here might be of some service to the elucidation of the difficulty. An animal is rendered unconscious by $CHCl_3$. The amount of $CHCl_3$ is increased. Eventually there is rapid failure of cardiac function, followed by a relatively gradual decline of respiratory movements. This is not invariably the course of the phenomena in these circumstances; but it is assumed as occurring on this occasion for the purpose of the argument. The animal being dead, the heart is cut out. The blood, under increased pressure in the right ventricle, escapes and relieves the organ of a mechanical encumbrance. The cardiac tissue, which is known to have great powers of resistance, is then subjected to stimulation. If, after the application of a stimulus varied in degree, the contraction is not appreciably different from that which follows the like degree of stimulation of a heart similarly

treated by an agency which is known to have no direct action in the cardiac tissue, evidence will be forthcoming in favour of the local nervous centres, and against the cardiac muscle, being the seat of the deadly action of $CHCl_3$—*i.e.*, on the supposition that the arrest of cardiac function has its origin in one or the other of these two components of the heart.

But there is a relationship between $CHCl_3$ and the action of the heart through the phenomenon of duskiness. Duskiness is one of the concomitants of pulmonic congestion. Pulmonic congestion is the cause of increased cardiac power. The initial energy of the heart, for it is not a constant quantity, tends therefore to be reduced. And it is obvious that the rate of reduction is greater in an initially weak heart than in one of normal strength.

How does $CHCl_3$ cause duskiness? This question was not considered by the supporters of the hypothesis. It is, nevertheless, one of importance. For in it is contained the solution of by far the greater part of the complex problem,—What is the relationship of $CHCl_3$-action to the heart?

In the course of duskiness accompanying the administration of $CHCl_3$, a fall of blood-pressure may occur. But the circumstances under which

it occurs vary. Thus, it occurs after a comparatively long period of the state of unconsciousness. Or it occurs soon after the induction of unconsciousness. In the former, the pupil is widely dilated when the pulse disappears, and this disappears not suddenly, but rapidly. In the latter, the pupil is partially dilated, and pulse-failure is sudden.

There is no difficulty presented in the explanation of rapid pulse-failure. It is characteristic of the "tired" heart. And it is not contrary to experience.

But the occurrence of sudden failure of the pulse during a degree of duskiness which, in the majority of instances, is associated with freedom from danger, is contrary to our experience of $CHCl_3$-action. What is the intervening source of disturbance? Is it the peculiar action of $CHCl_3$, or is it the result of a collateral cause acting simultaneously with $CHCl_3$?

Let us assume that there are two causes acting upon the heart—$CHCl_3$, and another which is not excluded by the supporters of the hypothesis. The possible causes of fall of blood-pressure are—1, primary cardiac syncope dependent on the action of $CHCl_3$; 2, reflex stimulation of the vaso-motor centre. Both these causes are associated with a sudden fall. Primary cardiac

syncope is always followed by the disappearance of the pulse, and is, on assumption, always fatal. Reflex stimulation of the vaso-motor centre is not always followed by the disappearance of the pulse. For the degree of stimulation varies, and the degree of fall of blood-pressure is in direct proportion to it. When a fall of blood-pressure happens, as the immediate consequence of reflex stimulation of the vaso-motor centre, the heart adapts itself to the new condition of the main circulation. Its action is reduced in proportion to the amount of blood diverted from the main circulation. When the fall of blood-pressure is severe, the function of the heart is reduced to a minimum.

What is the danger, then, that presents when fall in blood-pressure of vaso-motor origin happens during an abnormal condition of the heart, resulting from a moderate degree of pulmonic congestion? The present inability of the heart to overcome the obstacle in the circulation through the lungs. The obstacle requires increased cardiac power. The result of vaso-motor complication is the reduction of this power. Thus we have the operation of two causes acting in opposition. Either, when acting alone, is unequal to cause permanent arrest of the heart's action. But together they may.

Now, as all instances of sudden fall of blood-pressure are not fatal, it follows that the hypothesis is not universally true. And before it can be concluded to be true for all fatalities, it is requisite to exclude the co-operation of an independent cause.

In the case of the initial normal heart, there are three possible causes which may affect it during the action of $CHCl_3$—1, overwork; 2, reflex stimulation of the vaso-motor centre; 3, the assumed action of $CHCl_3$.

In the case of the initial abnormal heart, another cause is introduced—4, the origin of fall of blood-pressure is in the heart itself: there is the possibility of primary cardiac syncope.

All cardiac functional alterations are not invariably associated with alterations in blood-pressure in the relationship of antecedent and consequent. For when a fall of blood-pressure takes place, it may be related either primarily or secondarily to alteration in cardiac function —*i.e.*, a fall in blood-pressure may be either antecedent to, or consequent upon, cardiac change. It is incumbent, therefore, on the supporters of the hypothesis to exclude the presence of these causes, or, if any one or more of them are admitted to be present and

in operation when fall in blood-pressure occurs, to prove that they are unequal, alone or in combination, to produce the whole of it.

In the case of a complex condition, as of the heart, or respiratory machine or pupil, it is essential not only to isolate the causes, but also to determine how much of the result is due to each. The degree of action of any agent may vary within wide limits. Some are capable of being controlled. Others are beyond our control. Of two causes acting in combination, one may be predominant in one instance, the other in another. Thus, these two causes—respiratory overdose and mechanical obstruction — combine to cause arrest of respiratory movements. On one occasion, the respiratory overdose may be the chief causal factor; on another, mechanical obstruction.

Two causes, pulmonic congestion and primary fall in blood-pressure (*i.e.*, primary as regards its relationship to the heart), act in opposition to produce arrest of cardiac function. In one instance, there is severe degree of fall in blood-pressure and slight degree of pulmonic congestion. In another, there is moderate degree of fall in blood-pressure, and a relatively high degree of pulmonic congestion.

§ 7. *The imperfect treatment of the data entering*

into the solution of the problem.—Two conditions are assumed to represent the capricious action of $CHCl_3$: paralysis of the respiratory centre and cardiac depression. According to the hypothesis, either may be antecedent to the other, or both may occur simultaneously. $CHCl_3$ is absorbed into the blood, circulates in it, and, like an alkaloid, selects some parts of the organism for the seats of its action. But there is this difference between the operation of an alkaloid and that of $CHCl_3$. In the former, the results are uniform; in the latter, they are not. For example, in the case of strychnia, the first phenomenon indicating deadly action is invariably convulsion; and convulsion is followed by duskiness. But in the case of $CHCl_3$, the starting-point of dangerous action is not invariably in the heart, nor in the respiratory centre.

The chain of phenomena which antecedes failure of the pulse or of respiration is ignored as a means of explaining how crisis, or better, one group of crises, is induced. These phenomena are—1, Duskiness; 2, Increased action of the respiratory machine; 3, Commencing dilatation of the pupil. Initially of moderate degree, corresponding to the degree of $CHCl_3$-action, their tendency is (not to remain *in statu quo*, as might be inferred from the fact

that the original $CHCl_3$-overdose is maintained constant, but) to increase in intensity. The increase in their intensity is associated with the appearance of new phenomena. Thus, as the pupil increases in size it tends to become more and more sluggish; as the ordinary muscles of respiration become unequal to the exigencies of the increased work which they are called upon to perform, the extraordinary ones come to their assistance. Importance attaches to the rate at which the degree of these phenomena increases, in their forward course. One of the determining factors is the initial amount of $CHCl_3$—*i.e.*, the degree of overdose. If this degree be initially high, the rate of increasing intensity will be rapid. If it be initially moderate, the progress towards the termination of respiratory obstruction will be correspondingly slower. And thus it may happen that the progressive increase in intensity in the forward course of these phenomena, being so gradual, presenting such an insidious aspect, observation is deceived as to the value of their real nature. As matter of fact, then, there is uniformity in the course of $CHCl_3$-action, if we extend our study to the whole period of that action and not to one part of it only. The phenomena of respiratory or

pulse-failure, instead of being "isolated"—*i.e.*, the results of the direct action of $CHCl_3$ on the heart or respiratory centre—are thus connected with the antecedent chain, and either of them may be its natural terminal link.

The hypothesis of direct $CHCl_3$-action on the respiratory centre and heart was favoured by—1, not differentiating between different degrees of that action; and 2, by not including and explaining all the phenomena accompanying the higher degrees of it.

Duskiness is one of those phenomena. It is invariably associated with the higher degrees of $CHCl_3$-action. It varies in degree, and the variation of degree is in direct proportion to the variation of the degree of $CHCl_3$-action. But it is not a concomitant of all degrees of $CHCl_3$-action. It does not appear when the action is limited to the lowest degree of unconsciousness, which is called Anæsthesia. It is not, therefore, a necessary phenomenon accompanying $CHCl_3$-action. When it is present and is the antecedent of arrest of respiratory movements, the immediate object of investigation is the relationship between $CHCl_3$-action and duskiness, and not between $CHCl_3$-action and the respiratory centre. For there is a causal relationship between duskiness and arrest of respiratory

movements, the deoxygenated arterial blood leading to impairment of muscle-function.

The study of the causation of pulse-failure and of arrest of respiratory movements is, however, complicated by the intervention of causes acting independently of $CHCl_3$. Thus, there are two series of examples which are differentiated as follows: I. The action of $CHCl_3$ is not interfered-with: there is, therefore, a causal association between $CHCl_3$-action and failure of pulse or of respiration. II. The action of $CHCl_3$ is interfered-with by an independent cause, which has for one of its results either fall in blood-pressure or arrest of respiratory movements. The action of $CHCl_3$ cannot possibly be related to the whole result on the assumption that it is a causal factor, but only a part of it. The complex result may be chiefly caused by $CHCl_3$-action. On the other hand, it may possibly be chiefly caused by the complicatory cause.

Now there is a partial resemblance between examples of respiratory arrest, as also between those of pulse-failure. And this sufficed for the generalisation of the states of crises into two classes—I. Those beginning at the heart; and II. those beginning at the respiratory centre. But in neither group do the phenomena present

identical characters. The error underlying the generalisation originated in the inference that all instances of respiratory failure were caused in the same way, and were followed by the same consequences. Accurate observation detects differences in the modes of onset of arrest of respiratory movements. These differences are of fundamental value in the analysis of causation. The rational treatment of the phenomenon, arrest of respiratory movements, consists, then, of—1, consideration of the mode of its occurrence; 2, of the phenomena antecedent to it; and 3, of the phenomena consequential upon it; and these may have an early or late appearance. If, now, we apply this treatment to all the instances of arrest of respiratory movements, we shall find the differ ences to be as follows:—

A. The mode of onset is—

1. Sudden, and respiratory arrest occurs either during the act of inspiration or at the end of it; or,
2. The mode of onset is rapid.

B. The antecedent phenomena:—

1. Duskiness; increased action of the respiratory machine; dilatation of the pupil, becoming sluggish; progressive increase in intensity of all

these phenomena, leading to the action of the extraordinary muscles of respiration, and ending either in (*a*) rapid failure of the pulse, or (*b*) rapid decline of respiratory movements and their arrest.

2. Duskiness; increased action of the respiratory machine; dilatation of the pupil, becoming sluggish; in the course of the progressive increase in intensity of these phenomena (*a*) a change in the character of the respiratory movements, and (*b*) a change in the colour of the complexion occur. The latter appears to become pale, but is actually livid. At some point in the progress of this induced state, there is an attempt at full inspiration, during which the action of the respiratory machine is suddenly arrested.

3. Normal colour of the complexion; normal contraction of the pupil; efficient action of the respiratory machine. In the course of normal anæsthesia, there appear respiratory inhibition and pallor. During the course of those abnormal phenomena,

sudden arrest of respiration occurs at the end of a full respiration.

C. The consequential phenomena:—

1. There is no immediate alteration in the character of the pulse at the onset of respiratory failure. The strength of the pulse continues the same for two or three beats, after which it rapidly declines. The pupil is fully dilated and insensitive to light, before, during, and after the respiratory crisis. The degree of venous distension is increased.

2. Practically coincident with the occurrence of sudden arrest of the action of the respiratory machine, there is immediate fall of blood-pressure. The pulse may disappear (practically) simultaneously with respiratory arrest, or may flicker for a few seconds, and then disappear.

   The pupil, which is moderately dilated and sluggish before, becomes fully dilated immediately after sudden arrest of respiration. The degree of venous congestion, which is present before, is increased after the occurrence of respiratory complication.

3. Following upon sudden arrest of the action of the respiratory machine, there is (*a*) immediate fall of blood-pressure, leading to rapid but temporary disappearance of the pulse, and (*b*) immediate congestion of the venous system, which rapidly increases. The pupil remains in the condition of normal contraction. The contents of the stomach are expelled, after which there is a rapid return to the normal state.

The three characteristic differences which are displayed by the preceding analysis are:—

I. The mode of onset of the arrest of respiratory movements: it is rapid or sudden.

II. The attitude of the heart: there is immediate manifestation of change in the cardiac function in some instances; but only after an interval in others.

III. The attitude of the pupil: there is no alteration in some, but in others the pupil rapidly undergoes an increase in the degree of its dilatation. Now, the $CHCl_3$-hypothesis of respiratory arrest may be true. But whether it

be true or not, it is necessary to explain the differences characterising the phenomena which accompany inaction of the respiratory machine.

§ 8. *The significance of the increase in venous distension.*—Only one cause, cardiac contraction, can produce venous distension—*i.e.*, when it appears during the progress of $CHCl_3$-action. And it is the only cause that can add to it. When respiratory arrest occurs, the action of the heart is affected by abnormal conditions. These abnormal conditions may be favourable or unfavourable relatively to the inaction of the respiratory machine. They are favourable when, 1, the lungs are normal; and 2, the air-way is free from a temporary excess of $CHCl_3$-vapour. They are unfavourable when, 1, the lungs are congested; and, 2, the air-way is obstructed by an excess of $CHCl_3$-vapour.

When the cardiac action is rendered abnormal through arrest of respiratory movements, the amount of air in the air-way determines the rate at which the abnormality proceeds. Thus, in voluntary arrest of respiration, under normal conditions, there is no immediate effect on the pulse, for there is enough air in the air-way to subserve the function of aeration for two or three seconds. But the oxygen absorbed

is not replaced by the act of inspiration. When the amount of air present in the air-way begins to be unequal to the requirements of normal aeration, then the results of disturbance begin to appear. And that disturbance consists not in the immediate but gradual arrest of alveolar circulation.

The subsequent result upon the heart is distension of the right ventricle. Its progress is characterised by two stages—1, gradual increase of pressure in the right ventricle, corresponding to the gradual increase of obstruction to the alveolar circulation; 2, rapid increase when the obstruction tends to become complete. The cardiac contraction, being opposed in its normal channel—the pulmonic artery—directs its energy through the line of least resistance. The blood coming from the portal system is diverted into the superior vena cava, which is first the seat of distension. And its tension is progressively extended backwards in the course of the venous circulation, thus opposing the natural flow of blood towards the right auricle. As the result, there appears general venous distension.

If pulmonic congestion be present before the arrest of respiratory movements occurs, the course of events will be rendered more rapid. The heart is already obstructed in the per-

formance of the function. During this impaired condition, the obstacle—viz., alveolar obstruction, which is the cause of it—tends to become complete. Complete alveolar obstruction is reached sooner in the case of congested lungs than in that of normal ones. For there is a less proportion of air in the air-way to subserve the alveolar circulation. The degree of distension of the right ventricle, therefore, undergoes a rapid increase. The increase of venous distension appears early under these circumstances. When, on the other hand, distension of the right ventricle is slowly induced, a slight interval elapses before the superficial veins become distended. Under these circumstances, general venous distension appears as a late manifestation of cardiac obstruction. But whether it appears early or late, it signifies that the heart is endeavouring, under abnormal conditions, to perform its function, though there is no indication of it in the smaller arteries, for the pulse disappears as the alveolar obstruction tends to become complete. And as the result of this tendency is achieved more quickly in some instances than in others, an explanation is thus forthcoming of the different degrees of rapidity with which the pulse disappears. Thus the mere fact of disappear-

ance does not necessitate the conclusion that cardiac contraction has ceased.

§ 9. *The importance of accurate and complete data.*—When arrest of respiratory movements occurs, as it may do as well under innocent as under more or less unfavourable conditions, it is not sufficient to describe it merely as such, and to include all instances under the designation of "failure of the respiration," as if they were examples of one kind. For there are different kinds, depending on different causes. It is essential to record correctly the nature of the condition, which may be simple or complex, under investigation. This follows upon accurate and complete observation.

Thus a change in the colour of the complexion takes place. It appears to become pale. But the resulting condition is not, therefore, necessarily that of pallor.

The change which gives rise to the notion of paleness is arterial constriction, the consequence of fall of blood-pressure. Now this fall may occur during the presence of either, 1, duskiness; or, 2, the natural colour of the complexion. In the former contingency, the complex condition of lividity will appear, in the latter the simple one of pallor. There is a tendency to mistake lividity for pallor on some

occasions. A predisposition to the error exists in the original natural colour of the complexion. In order to avoid it, differentiation of the conditions under which "paleness" occurs is to be made. If the superficial veins are distended, no matter how pale the complexion may seem, the condition is that of lividity. If, on the other hand, the veins are not distended, the condition is that of pallor. The differentiation is of first-rate importance. For if the complexion is actually livid, but only one component of the abnormal condition is taken into consideration, viz., arterial constriction, while the others, venous distension and discoloration of the blood, are ignored, the possibility arises of inferring a false cause from a single character which is not fundamental. Fall of blood-pressure is one of the terminal results of physiologic pulmonic congestion; venous distension is an indirect result of the same cause. It is requisite to disprove causal relationship between these two factors when they coexist. The conditions which relate them as indirect results of the same cause are known. They are—1, antecedent, increased, and increasing action of the respiratory machine, leading to (*a*) some degree of exhaustion of the ordinary muscles of respiration, and (*b*) the coming into

action of the extraordinary ones; and, 2, the characteristic mode of fall of blood-pressure. It is rapid, not sudden. Fall of blood-pressure, however, may occur during duskiness, when those conditions are not present. Hence it might be inferred that duskiness is not causally related to fall of blood-pressure during $CHCl_3$-action, the ground of the inference being that paleness occurs both when duskiness is moderate and when it is extreme. A reason is consequently advanced for assuming that the same cause is in operation to produce fall of blood-pressure during different degrees of duskiness. And certainly, if $CHCl_3$ is the ultimate cause, it matters nothing whether there be any degree of duskiness, or whether there be no duskiness at all.

But the assumption that the cause of falls of blood-pressure occurring during different degrees of duskiness is one and the same—viz., $CHCl_3$-action—excludes the possibility of another cause being in operation and producing the same result. This cause is reflex stimulation of the vaso-motor centre. It is associated, when sufficiently intense, with sudden failure of the pulse. Now this mode of fall of blood-pressure is identical with that which takes place, in some instances, but not all, of pulse-failure

during a moderate degree of duskiness. We have, therefore, the action of $CHCl_3$ associated with two different modes of onset of failure of the pulse,—sudden and rapid. It is necessary to explain why, in some instances, the failure is rapid, in others sudden. The following analysis is subservient to this end.

The cause of duskiness is pulmonic congestion, the result of the negative action of $CHCl_3$.

The causes of fall of blood-pressure are—1, tired heart; 2, reflex stimulation of the vaso-motor centre; and 3, primary cardiac syncope, an assumed result of $CHCl_3$-action.

There is a causal relationship between duskiness and fall of blood-pressure. It is determined by known conditions. The mode of onset of the fall is invariably rapid.

There is no causal relationship between duskiness and fall of blood-pressure. The cause of the latter is independent of the action of $CHCl_3$. It is either, 1, reflex stimulation of the vaso-motor centre; or, 2, primary cardiac syncope. Both these are invariably associated with sudden failure of the pulse.

The surroundings of the heart, when fall of blood-pressure occurs during duskiness, are not favourable to the resumption of its function in

a case of vaso-motor disturbance For there is an obstacle opposed to it, in the presence of some degree of pulmonic congestion, interfering with the passage of the blood from the right to the left ventricle. In such circumstances stimulation of the heart is contra-indicated. What is indicated is the removal of the obstacle, and its immediate removal. For delay in this respect has but one tendency—viz., towards cessation of cardiac contraction.

§ 9 *a. The order in time in which phenomena appear.*—Another point, in which accuracy of observation is of paramount importance, is the order in time in which two or more phenomena appear. For the rational study of causation is not restricted to the treatment of one phenomenon — it includes all the phenomena. For example, a variation occurs in the action of the respiratory machine. Respiratory variation is invariably followed by variation in the circulatory system. It may be followed by variations in the character of the blood and of the pupil. Thus different sets of phenomena are presented. It is the same with variations in the circulatory system. All circulatory variations are not necessarily followed by the same set of phenomena. Now there will be a tendency to uniformity in the phenomena, con-

sequent upon variation in the circulatory system, if the cause of variation be always the same. The absence of uniformity, therefore, may be adduced as evidence in favour of a cause, or causes, operating independently of the action of $CHCl_3$.

There is an interval of time, which varies in length, and in some instances is so short as to be ordinarily inappreciable, between the antecedent phenomenon and the consequent phenomena. Variations occur apparently simultaneously in the respiratory and circulatory systems. A fall of blood-pressure of moderate degree is observed to be associated in one instance with inhibition of the breathing. The like degree of fall of blood-pressure is associated, in another instance, with respiratory acceleration. Which is the antecedent and which is the consequent phenomenon in these two instances?

The determination of the antecedent phenomenon is of the highest moment, inasmuch as it points to the ultimate source of complication. And in this way it reacts against the tendency towards regarding pallor as being necessarily the more important phenomenon, when it is associated with respiratory variation in the course of $CHCl_3$-action. The right treatment consists in giving to each phenomenon its proper

value. What, then, is the value of any one respiratory variation?

Now the founders of the $CHCl_3$-hypothesis did not take into consideration the minor degrees of variation in the action of the respiratory machine. They regarded but one degree of it, and that an extreme one—viz., its failure. So long as breathing was continuous, no matter what its character might be, there was no evidence of paralysis of the respiratory centre. The respiratory machine exhibited an activity greater than the normal. But instead of this abnormal activity being regarded as an undue consumption of motor-power, it was taken to be a favourable indication. For the respiratory machine was acting well, and that was so. But under what conditions? Because it acts well for a given period, under unfavourable conditions which do not vary very much, or if they do, vary but slowly, is it proper to assume that it will act as well during a subsequent period, when those conditions present a marked increase in their intensity?

This minor variation—viz., the abnormal activity of the respiratory machine—is of value in that it leads to the investigation of its cause—viz., pulmonic congestion. Pulmonic congestion is associated with the higher degrees

of $CHCl_3$-action. It is not associated with the anæsthetic degree. When that abnormality in the action of the respiratory machine is present, it is made to disappear by putting out of operation its ultimate cause—*i.e.*, by reducing the high proportion of $CHCl_3$ in the mixed $CHCl_3$-air atmosphere to the anæsthetic proportion. There are two kinds of respiratory variation which may occur during any degree of $CHCl_3$-action, but are most clearly defined when that action is limited to the anæsthetic degree. They are inhibition and acceleration. Their appearance is occasional. And when they do appear, their duration is not conterminous with the whole period of $CHCl_3$-action. They are invariably associated with pallor. Let us examine these associated phenomena—viz., respiratory inhibition and pallor, and pallor and respiratory acceleration—from a purely physiological standpoint, and thus dissociate them from $CHCl_3$-action.

Reflex stimulation of the vaso-motor centre is immediately followed by pallor—*i.e.*, fall in blood-pressure. Pallor is immediately followed by respiratory acceleration. Here pallor is the antecedent, respiratory acceleration is the consequent, phenomenon.

Inhibition of the respiratory centre is im-

mediately followed by, 1, a reduction of the power; and, 2, a diminution in the frequency, of the respiratory machine. These are the components of the kind of breathing called respiratory inhibition, which is immediately followed by pallor. Here respiratory inhibition is the antecedent and pallor the consequent phenomenon. Pallor may thus be either the antecedent or the consequent when associated with respiratory variation. How is its nature determined when the two phenomena occur practically simultaneously? The vagus nerve may be intentionally stimulated, in a physiological experiment; and so may a branch of the sympathetic nerve. The cause is thus isolated. It is associated with recorded phenomena, and it is proved by subsequent experiments to be invariably associated with the same phenomena.

But the case is different when these phenomena occur in the course of $CHCl_3$-action. For the sympathetic nerve is not intentionally stimulated, and when the mucous membrane of the stomach is examined, the intention is not (incidentally) to perform a simple physiological experiment. There is, however, a means of differentiation. It resides in the character of the respiratory variation, and it is in this that

the value of the respiratory variation consists. When pallor appears associated with shallow accelerated breathing, the inference is that reflex stimulation of the vaso-motor centre is present. For a moderate degree of stimulation of the vaso-motor centre is invariably followed by this particular action of the respiratory machine. The order of the phenomena may then be inferred to be antecedent pallor, consequent respiratory acceleration. On the other hand, when pallor is associated with respiratory inhibition, the order is reversed. It is known that inhibition of the respiratory centre is followed by sympathetic disturbance in the vaso-motor centre, which is expressed in a fall of blood-pressure and manifested by the appearance of pallor. Under the conditions, and excluding $CHCl_3$-action for which is claimed not inhibition but paralysis of the respiratory centre, there is no other known cause of respiratory inhibition than direct stomachic disturbance, consisting in the stimulation of the terminal branches of the vagus.

When this stimulation ceases—*i.e.*, the respiratory centre is released from inhibition—the circulation immediately begins to return to the normal, which it reaches very rapidly. And $CHCl_3$ may have been continued during the

whole duration of the complication (but with the requisite modification in the method of administration, adapted to the abnormal action of the respiratory machine). The rapid return to the normal, when there is no intervening impediment, characterises the abnormal state of vaso-motor depression occurring during $CHCl_3$-action. Rapid return to the normal is associated with reflex action. The pulse disappears during $CHCl_3$-anæsthesia. It reappears naturally, and reaches within a period of 50″ or less, the degree of tension it exhibited before the occurrence of complication. During moderate degrees of fall of blood-pressure, $CHCl_3$ may be continued. But the amount is to be accurately adjusted to each stage of the complication.

The attitude of the heart in this group of complications contra-indicates the presence of an agent exercising a depressant influence on its function. For if it were depressed to such a degree as is measured by pulse-failure, it would require a much longer interval than 50″ in which to recover its normal tone. But it is possible that the cardiac action may be rendered abnormal before primary fall in blood-pressure occurs. When this combination arises, an obstacle is placed in the way of the natural

recovery of the heart. Recovery is necessarily prolonged. And the surrounding conditions may be so unfavourable as to prevent it. These are some of the examples that led to the plausible conclusion that $CHCl_3$ acted directly on the heart.

§ 10. *Crises.*—The onset of crisis is—1, sudden; 2, rapid; or 3, gradual. There is no uniformity in the phenomena, anteceding or accompanying it, nor in those which follow upon it. But if, instead of deducing $CHCl_3$ to be the cause of all these irregularities, we classify them into groups, according to the less or greater degree of resemblance which exists among some of them, and serves to differentiate them from others, uniformity will then appear in the different examples of the same group. For example, it is observed that in all instances of primary arrest of respiratory movements, the pupil is either contracted or dilated (but the degree of dilatation is not always the same). Two subdivisions are thus formed. But both these subdivisions may be associated either with a normal or abnormal state of the respiratory machine. Consequently, four groups are formed. The process of differentiation, however, does not end here. For this reason. There are different abnormal states of the respiratory machine. Each of the two

groups, which are characterised by abnormal action of the respiratory machine, is then to be further divided into sub-groups, according to the nature of the abnormality.

Thus, we arrive at different sets of phenomena, which have for their common factor arrest of respiratory movements. But, 1, the dilated pupil may be fixed or sluggish or sensitive to light; and, 2, the mode of onset of respiratory arrest differs. The character of the dilated pupil, and the mode of onset of respirtory arrest, have thus to be defined in order to complete the system of generalisation.

With regard to primary fall of blood-pressure, the analysis is not so complex. It occurs during either a normal or an abnormal state of the circulatory system. In the latter case it is one either of minus or plus arterial tension. Dilatation of the pupil is invariably associated with primary fall of blood-pressure. But the degree of it varies. It is moderate when the degree of fall of blood-pressure is moderate. It is fully dilated when the fall is severe—*i.e.*, when the pulse disappears.

The components of the state of crisis are to be treated in their entirety. It is not, however, proper to conclude that either the failure of the pulse or of the respiration, whichever appears

first, of itself points to the origin of the complication. For sudden arrest of respiratory movements is not necessarily the consequence of primary affection of the respiratory centre, and rapid failure of the pulse may be but an accidental phenomenon, one of the two natural terminations of a complicatory cause, created by the negative action of $CHCl_3$.

The state of crisis may be dependent on $CHCl_3$-action. But $CHCl_3$ has three separate actions, which may either individually or in combination be associated with crisis. It is necessary, therefore, to define the particular action or actions of $CHCl_3$ in each individual instance of this group of crises, and, in the case of its physiological action, to isolate the part of the organism which is directly affected.

Evidence might be adduced, were it required, to the effect that the vast majority of instances of crisis are not due to the deadly action of $CHCl_3$, at any rate in the sense in which it is used. For it is a matter of extreme difficulty to induce a pure $CHCl_3$-crisis; and without the co-operation of some agent acting simultaneously with, but independently of it, to induce any crisis at all: and then it is only possible where $CHCl_3$ is acting in an abnormal degree. "What

part $CHCl_3$ plays in the causation of crisis" becomes thus a proper ground of investigation. Of two or three causes acting together it may either be the chief one, or co-ordinate with or subordinate to another. Acting alone, it is known not to be associated with the appearance of "grave" phenomena. But these occur, and rapidly become critical. The questions then arise: 1. Is the appearance of these grave phenomena always associated with crisis? 2. If crisis is present, is it always of the same degree? Crisis does not invariably follow the occurrence either of failure of the pulse or of respiration. And it is curious to note that instances of extreme pallor recover with the greatest rapidity. But there may be misapprehension as to the actual state of the complexion. An example of lividity is mistaken for one of pallor. Now it is lividity that is associated with danger, which may be immediate. Recovery in such a case is not rapid, but follows after a longer or shorter interval, which is determined by the initial degree of venous distension. (And artificial assistance may be required.)

The components of the condition of lividity are, 1, arterial constriction, the consequence of fall of arterial blood-pressure; and, 2, cyanosis. The components of cyanosis are, 1, discolor-

ation of the arterial blood; and, 2, venous distension.

Cyanosis is associated with the negative action of $CHCl_3$. The degree of the one is directly proportioned to the degree of the other. When cyanosis is not present during $CHCl_3$-action (*i.e.*, the action of $CHCl_3$ is limited to the anæsthetic degree) and fall of blood occurs, there is no danger; when cyanosis is present during $CHCl_3$-action (*i.e.*, the action of $CHCl_3$ is represented by some degree of narcosis) and fall of blood-pressure occurs, some degree of danger is introduced. Cyanosis is the result of pulmonic congestion. It is the disturbing factor which is associated with the occurrence of crisis. For it opposes an obstacle to the progress of the natural but abnormal functions of both the stomachic and vaso-motor systems.

§ 11. *Abstract treatment of the evidence forming the basis of Hypothesis.*—In the original treatment of the states of crisis, all instances of arrest of respiratory movements were regarded as being of the same value. But differences were observed—*e.g.*, in the mode of its onset,—sudden in some, rapid in others; and the explanation of these differences might very well have formed the starting-point of a fresh and collateral inquiry. For they may or may not be character-

istic. Their presence, however, only tended to accentuate the peculiar action of $CHCl_3$. The same treatment was applied to instances of pulse-failure. Thus generalisations were drawn not from similar states, but from states which were assumed to be similar. A fundamental error was introduced into the investigation of $CHCl_3$-action. The knowledge of this action, however, is not derived from all examples of crisis. Hence the importance of dissociating $CHCl_3$ from their initial causation. For it opens up the way to the operation of independent causes. As in the instance of any other agent, knowledge of $CHCl_3$-action is derived from the phenomena which generally accompany it, not from those which occasionally do so. And as all agents are capable of undergoing variation in the degree of their action, so is $CHCl_3$. Now the higher degrees of this action tend to mask the true nature of the complicatory cause which comes into operation, not at a definite, but very irregular, period during its administration. For example, the action of the respiratory machine becomes inhibited. This abnormal condition is followed either by, 1, sudden arrest, the interval being so short between inhibition and arrest that the former may pass unnoticed; or, 2, by rapid arrest. The key

to the solution of this part of the $CHCl_3$-problem is "respiratory inhibition." Sudden arrest is known to be causally related to it. The action of the respiratory machine is reduced as the result of the temporarily disturbed function of the respiratory centre. The $CHCl_3$-air atmosphere is consequently moved by less power. But $CHCl_3$ is a heavy vapour. The tendency towards producing an impediment in the action of the respiratory machine which was checked by an increase in its activity now becomes operative when that activity is diminished. And the greater the proportion of $CHCl_3$ the more quickly the final result of respiratory impediment appears—viz., arrest of respiratory movements. There is, then, a physical cause which explains not only the mode of onset, but also the variations in the degree of rapidity of occurrence of respiratory arrest.

Now, arrest of respiratory movements is not, under these conditions, followed by natural recovery. But they are artificially restored by removing, 1, the physical impediment in the case of rapid arrest—*i.e.*, complete obstruction during inhibited respiration; and, 2, the pulmonic impediment in the case of sudden arrest—*i.e.*, reflex suspension of the function of the respiratory centre during pulmonic congestion.

But the course of the complication, commencing with respiratory inhibition, is clearly and distinctly portrayed during $CHCl_3$-action, limited to the degree of anæsthesia, when the method of administration is adapted to meet the requirements of the abnormal condition of respiration. In these circumstances the inhibited character of the breathing continues for a longer or shorter period, at the end of which it is suddenly interrupted by respiratory arrest on the completion of a full inspiration. The expulsion of the contents of the stomach follows, after which there is a rapid return to the normal state. This rapidity of the return to the normal is the characteristic of reflex-action.

§ 12. *The complexity of the Respiratory and Circulatory Systems.*—Variations in the action of the respiratory machine and in the state of the circulation may proceed from other causes than disturbances respectively in the respiratory centre and heart. The air-way may be obstructed, 1, by the base of the tongue being displaced backwards; and, 2, by the physical action of $CHCl_3$ (respiratory overdose). The lungs may be in a condition of physiologic congestion. The muscles of respiration (the motor-power) may become exhausted. All these causes affect, each in its own par-

ticular way, the action of the respiratory machine. The circulation may be rendered abnormal through changes in, 1, the cardiac function; and, 2, the vaso-motor system.

The higher degrees of $CHCl_3$-action are associated with an abnormal state of the respiratory machine. If another cause which affects that machine comes into operation when it is in a state of abnormality, the resultant condition is not simple but complex. In order to measure what the result of the collateral cause is, it is necessary to define what changes are effected by $CHCl_3$. These changes vary with varying degrees of $CHCl_3$-action. In the case of $CHCl_3$-anæsthesia, there is only one change—viz., increase in the frequency of respiration.

The result of $CHCl_3$-action limited to anæsthesia on the respiratory machine being thus determined, any additional variation can easily be observed in the course of the constant state of $CHCl_3$-anæsthesia. Suppose a variation to occur. Its character is noted. The phenomena which accompany it are recorded. The data are thus collected which lead to the detection of the source of disturbance. But suppose an abnormal condition of the respiratory machine to be present when variation

occurs, the analysis of causation becomes in consequence intricate. The essential data are then as follows:—

(i) The nature of the abnormal condition of the respiratory machine at the onset of variation. The particular mode of onset, and the progress of the variation.

(ii) The determination of the relationship between the abnormal condition and the variation. They may or may not be causally related.

(iii) If a causal relationship exists, to proceed to the further determination, whether it explains the whole result or only part of it. This leads to the isolation of a cause co-operating with $CHCl_3$ to produce the same result.

(iv) If there is no causal relationship, to collect the data which lead to the detection of the cause acting simultaneously with $CHCl_3$.

(v) The determination of the relationship of this to $CHCl_3$. It may be indirectly dependent on $CHCl_3$-action—*i.e.*, a direct $CHCl_3$- result becomes an intermediate cause, or it may be independent of the action of $CHCl_3$.

It is only by this procedure that error is avoided at each step of the investigation.

Variations in the degree of $CHCl_3$-action occur in the progress of the induction of $CHCl_3$-anæsthesia. Under these circumstances there is no constant state of $CHCl_3$-action. Towards the onset of anæsthesia there occurs arrest of respiratory movements at the end of expiration. Up to the moment of arrest the action of the respiratory machine has been efficient. And when arrest takes place, the pupil is normally contracted. What is the cause of respiratory arrest?

The same amount of $CHCl_3$, administered in the same way,—the normal method of inducing anæsthesia,—is not invariably associated with the occurrence of respiratory arrest at that particular time, nor, it may be added, at any other. The cause of that phenomenon is either in some part of the respiratory machine or in the respiratory centre. But there is no evidence of any abnormality affecting the respiratory machine when arrest of its action takes place. There is neither mechanical obstruction nor pulmonic congestion; for both these factors are associated with duskiness—*i.e.*, inefficient action. There is no respiratory over-dose of $CHCl_3$ which is effective, for it is also associated with duskiness.

There is no muscle-exhaustion, for this condition is the consequence of prolonged increased activity. By this process of exclusion the source of arrest is confined to disturbance in the respiratory centre. Now, this centre may conceivably be affected by, 1, voluntary arrest of its function, for the patient is not yet completely unconscious, and the will-power is one of the last of the mental functions to be suspended, if it be not the last; and, 2, $CHCl_3$-action. The determination of the cause is effected by the subsequent progress of the phenomena. The action of the respiratory machine continues "arrested" for a period of 8″, during which the complexion undergoes a change. It gradually but progressively becomes dusky. The pulse gradually diminishes in frequency and increases in strength. The pupil, however, remains normally contracted throughout. At the termination of the period of arrest the respiratory machine at once resumes its normal function. And in this respect comparison may be made between the present example and others in which the recovery of function is gradual.

The immediate resumption of its normal activity proves that the respiratory centre has not been in a condition of depression—*i.e.*, its

vitality has not been affected by the direct action of $CHCl_3$ on it. For, if such had been the case, the centre would have required some interval of time in which to recover from the results of depression, and the process of recovery would necessarily be slow. Seeing that, in this case, the degree of disturbance is associated, not with a diminution but an arrest of functional activity, recovery would require a comparatively long period. And the initial indication of returning function would be manifested not in vigorous but in faint movements of the respiratory machine.

The course which the centre of respiration takes in this case is thus not in conformity with experience derived from direct action of agents upon nerve-centres.

There remains, then, the voluntary act of arresting respiration. This is known not to be associated with a corresponding sympathetic result in the circulatory system. The pulse undergoes a change, which progressively increases, answering to the progressive increase in the impairment of the function of aeration, consequent on the inaction of the respiratory machine.

Voluntary arrest of the function of the respiratory centre is followed, immediately on its re-

lease from the influence of the will, by normal respiration, when the conditions affecting the respiratory machine are not unduly abnormal. Both voluntary inhibition and arrest of the action of the respiratory centre are common occurrences in the early stage of the induction of anæsthesia. The centre is generally released by voluntary act before the attainment of unconsciousness. But if voluntary arrest takes place in the later stage, there is the chance that unconsciousness may supervene before the release of the centre has been effected. In such a case the arrest of respiration is the last act of volition.

Now, a lower centre, acted upon by a higher one, continues in the state of disturbance which has been created in it, after the suspension of the function of the latter. But not in the same degree. For the amount of disturbance progressively declines. As soon as the results of disturbance in it disappear, the lower centre is capable of resuming its function at once and normally. This, in the case of the respiratory centre, presupposes the absence of impediment (except such as are consequent upon the arrest itself) in any one or more of the components of the respiratory machine. It is conceivable that, at the moment of voluntary arrest of respiration,

the state of the respiratory machine may be abnormal. The course of events will then be determined by the nature and degree of the abnormal condition or conditions which are present.

§ 13. *Inductive Investigation.*—When a variation in kind takes place in an abnormal state of the respiratory machine, the result is complex. To mistake a complex for a simple result is to introduce a fundamental error into all inferences that may be derived from it. The prevalence of this error accounted for one of the many sources of perplexity surrounding the study of the $CHCl_3$-problem. The first series of observations was confined to the phenomena which were associated with the action of $CHCl_3$ administered under these conditions. Three drops were given at intervals during the first minute, after which the amount was immediately raised to the maximum, which was 10 drops. With this slight modification of the Rapid Method, muscle-phenomena were of general occurrence. Their absence was the exception and not the rule. When the breathing became automatic, the following were the phenomena presented by the patient. The complexion was invariably dusky. The pupil was invariably dilated; but there were differences in the de-

gree of dilatation. The pulse was slower than normal, and was characterised by increase in tension; but there were variations in the degree of diminution in frequency. The colour of the arterial blood was dark, the degree of discoloration not being constant. The action of the respiratory machine was increased both in vigour and frequency, and this increased activity was regarded as the sign of the normal action of $CHCl_3$.

Thus different degrees of the state of narcosis were induced and maintained, the degrees being differentiated by, 1, size of the pupils; and, 2, greater or less discoloration of the arterial blood.

But in the course of the maintenance of this state of narcosis, it was observed that the phenomena did not remain constant. There was a tendency towards a rise and fall in their degree. The rise invariably followed upon the addition of $CHCl_3$, the quantity of which was kept constant, and repeated at the end of 3′. Thus, with an increase in the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere, the pupil became appreciably larger and the discoloured blood appreciably darker. As the proportion of $CHCl_3$ diminished, partly through absorption, partly through evaporation, the pupil became smaller and the blood less dark.

A relationship between the action of $CHCl_3$ and the pupil was thus isolated, and expressed in the following terms: As the degree of $CHCl_3$-action tends to increase, the moderately dilated pupil becomes more dilated; as the degree of $CHCl_3$-action tends to diminish, the dilated pupil becomes smaller. The significance of this relationship was, however, obscured by the following considerations. 1. Variations of the degree of dilatation occur independently of the rise and fall in the amount of $CHCl_3$ absorbed. What is the origin of these accompanying changes? 2. The tendency towards successive periods of rise and fall is not the only one present. It has an associate which is not readily isolated during short periods, but is very easily isolated during long periods of $CHCl_3$-action. It is the tendency towards gradual but progressive increase in dilatation. The first series of experiments were undertaken with the object of determining the results of a variation in the method of administration. Instead of immediately increasing the proportion of $CHCl_3$ to the maximum after the short initial period, during which a relatively small proportion is operating, an alteration was adopted so as to introduce $CHCl_3$ more gradually into the system. The short initial period was therefore prolonged.

The results of this variation were as follows. First, the appearance of a marked diminution in the frequency of muscle-phenomena. Secondly, there was a tendency towards the formation of two groups which were differentiated by the size of the pupil. Between the two extremes, however, of large and small pupil, there were some instances which presented intermediate degrees of dilatation. And the conclusion was drawn that the same amount of $CHCl_3$, administered in the same way, was, in the majority of these cases, accompanied not by like, but by unlike, results so far as the pupil is concerned.

The course, however, of this investigation was marked by the occurrence of exceptional instances. They differed from the majority in the following points: 1. The absence of muscle-phenomena; 2. The onset of automatic respiration, before the arbitrary maximum amount of $CHCl_3$, for the determination of the actual maximum was not as yet regarded as being of primary importance, was reached. In all of them the pupil was contracted. The state of unconsciousness was afterwards maintained by the use of (not the arbitrary maximum, but) the proportion which had been reached when automatic respiration supervened.

The isolation of this exceptional group led to a second series of experiments. It was suggested that if 7 or 8 drops as the maximum in a constant $CHCl_3$-air atmosphere were sufficient for some cases, they might suffice for all. But it was feared that a reduction of the then maximum amount would probably, in the majority of cases, exercise too great an interference in what was considered to be the normal course of events, if applied to the stage of induction. The variation was, therefore, in the first place restricted to the stage of unconsciousness. Thus, unconsciousness having been attained by the maximum amount of 10 drops, administered at such intervals as to produce a nearly constant $CHCl_3$-air atmosphere, and maintained for a period of 10′, in order to introduce stability into the conditions (or, more accurately, to make them as stable as they can be made by the regular administration of $CHCl_3$), the maximum dose was then reduced to 7 drops. The results following this experiment, in a large number of cases, were remarkable in that they exhibited uniformity. In all the pupil, whatever its initial size might be, and it was always more or less dilated, became smaller. In all the discoloured arterial blood, whatever its degree of discoloration might be, became less dark. These varia-

tions in the size of the pupil and of the colour of the blood, associated with a reduction of the amount of $CHCl_3$, do not, however, reach their extreme degree immediately. The progress towards a lower degree of dilatation is gradual, as is also that towards a lower degree of discoloration of the blood.

Now, this reduction in the amount of $CHCl_3$ was not attended by any unfavourable consequences so far as the surgical operation was concerned. It was decided, therefore, to continue the experiment by further reducing the amount of $CHCl_3$. And, acting on conservative lines, the procedure adopted was a gradual one. First 10 drops were reduced to 8 drops soon after the onset of automatic respiration; and after 8 drops had been continued for 10′, they were reduced to 6.

The variations observed in this series were exactly the same as in the former. With the reduction from 8 to 6 drops the pupil became gradually smaller, just as it did when the amount was reduced from 10 to 8 drops, and the discoloured blood became gradually less dark. From these two series of experiments the following conclusions necessarily proceed. I. As the proportion of $CHCl_3$ is progressively diminished, the pupil becomes smaller and the

discoloured blood less dark. II. There is a relationship between the degrees of the antecedent (viz., variation in amount of $CHCl_3$) and the degrees of the consequents (viz., size of pupil and the discoloured blood): thus the same degree of reduction in the amount of $CHCl_3$ is always associated with the same degree of diminution in the size of the pupil as well as with the same degree of change in the abnormal colour of the arterial blood.

During the course of these experiments the same tendency as had previously been observed in other series of experiments towards progressive dilatation of the pupil (apart from variations in it, associated with variations in the amount of $CHCl_3$) was invariably exhibited. The degree of $CHCl_3$-action is reduced to 6 drops. The pupil is correspondingly reduced in size. But with the regular administration of $CHCl_3$ at this new maximum, the pupil, instead of remaining the same, undergoes a change. It gradually dilates. This tendency, then, introduces the following difficulty. The same degree of $CHCl_3$-action is associated, at different periods of the progress, not with the same, but with different sizes of the pupil. If, now, $CHCl_3$ be regarded as the cause of the dilatation of the pupil—and it is matter of fact that differ-

ent degrees of $CHCl_3$-action are associated with different sizes of the pupil—the hypothesis is at once assailed by the contradiction that the same degree of cause is not always associated with the same degree of effect, on the supposition that the condition of the iris remains the same throughout the administration. But it may not do so. Two possibilities are, therefore, presented. Either the relationship between $CHCl_3$ and the dilated pupil is direct, and then the condition of the iris does not remain the same, but becomes less resistant to $CHCl_3$-action; or the relationship is indirect—*i.e.*, there is an intermediate cause which directly affects the iris in such a way as to lead to a tendency towards dilatation of the pupil.

The experiment of diminishing the degree of the maximum amount was next applied to the stage of induction. At first diffidence was associated with change in the then customary method of conducting the administration of $CHCl_3$. It arose from a prevailing belief in the precept that a severe operation required a greater degree of narcosis than a slight one. Consequently, cases of minor operations were selected.

The maximum was reduced to 8 drops. And the method of administration was modified so as to reach the maximum at a less degree

of rapidity than had been practised in the previous series. Thus, one drop was repeated at short intervals for 30″; after which two drops were continued in a like manner for 1′, when the amount was raised to 4. The increase in concentration was afterwards more rapidly induced, but not so rapidly as formerly.

Examination of the records obtained from a series of cases treated by this modified method showed—

1. A tendency towards the appearance of quietness during the early stages of the administration. The so-called state of excitement occurred, followed by muscle-phenomena; but instead of coinciding with the commencing action of $CHCl_3$, as formerly, they appear after $CHCl_3$ has been in operation for a clear interval. The modified method is thus associated with the postponement of these phenomena. Their occurrence, when they appear, for they do not always appear, is associated with the second stage of the method—viz., that which is characterised by "rapidity" in the increase of $CHCl_3$ up to the maximum.

2. There is a decrease in the number of instances of muscle-phenomena. At the same time, a tendency towards diminution in their intensity appears.

3. When unconsciousness is attained, the average size of the pupil is found to be smaller than in the series with 10 drops as the maximum—*i.e.*, there is a less degree of its dilatation. The colour of the blood is also, in comparison of the degree of its discoloration in that series, less dark.

These results, associated with diminution in the amount of $CHCl_3$, show that a very considerable amelioration in the state of the patient had been induced. The variation in method in no way interfered with the exigencies of minor surgical operations. As, however, the state of unconsciousness had in the former series been maintained by the use of a minimum of 6 drops, regularly administered at intervals of 1′—and as in the present series the maximum of 8 had been reduced to that mimimum—the suggestion occurred that if 6 drops, regularly continued, suffice to maintain unconsciousness, the same amount, substituted for the former maximum of 8 drops, and applied in accordance with the principle of the modified method, might be sufficient to induce unconsciousness. In order to test the validity of this suggestion, a further series of experiments were conducted under the following conditions—1, modified method; 2, reduced maximum of 6

drops. (The plan of gradually increasing the proportion of $CHCl_3$ was, in this series, extended to the whole period of induction.)

The collation of the records thus obtained brought out the fact that the group of muscle-phenomena, which formerly contained nearly all cases, was reduced to a comparatively small percentage. Instead of being represented by 90 per cent, it was now represented by 10 per cent. This change of proportion is associated with two variations—1, diminution of the maximum amount of $CHCl_3$; 2, the gradual increase in the proportion of $CHCl_3$ in the mixed $CHCl_3$-air atmosphere up to the maximum. But the fact remained that muscle-phenomena might still accompany these variations. Their causation became the object of subsequent investigation.

A second tendency which was brought into view, was towards a further diminution in the size of the pupil. In a few instances it was nearly pin-point, and in these it was observed that as the action of the respiratory machine became regular the pupil began to contract and continued contracting, up to the onset of automatic respiration, when it was seen to be nearly pin-point.

A third tendency was connected with the

blood. Its colour approached the normal. In the instances where the pupil was nearly pin-point, no difference could be detected between the colour of blood which was being affected by $CHCl_3$ and that of normal arterial blood. In fact, in these few instances normal anæsthesia had been induced. But it was not maintained. For the maximum amount being continued at 6 drops, the same tendency appeared as has already been demonstrated to exist in former series of experiments—viz., towards dilatation of the pupil and discoloration of the blood. But with this difference, with a large maximum—*e.g.*, 10 drops—the rate of progress of these phenomena is relatively quicker than with a small one—*e.g.*, 6 drops. The results of the improved modified method being favourable in minor, it was decided to use it in major, operations. In these, too, it was equally successful.

§ 14. *Summation of Results.*—1. There are different degrees of $CHCl_3$-action, which are determined by the size of the pupil and the colour of the blood. 2. In a few instances, the degree of $CHCl_3$-action is associated with contracted pupil and normal colour of the blood. 3. The same proportion of $CHCl_3$ being continued, the results associated with it do not

remain the same, but undergo a progressive increase. 4. Muscle-phenomena do not completely disappear.

In the course of these experiments, instances of arrest of respiration occurred during the stage of induction, and of arrest of respiration and pulse-failure in the course of unconsciousness. The object of these series of experiments was the isolation of the phenomena associated with the ordinary, as distinguished from what was termed the extraordinary, action of $CHCl_3$. The former are restricted to variations in, 1, the size of the pupil, and, 2, of the colour of the blood, with the view of simplifying the course of the investigation. But the variations of all the phenomena accompanying alteration in the degree of $CHCl_3$-action were accurately observed and correctly recorded. They include variations in, 3, the action of the respiratory machine; 4, the action of the heart, manifested by the pulse; 5, the venous system; and 6, the muscular system.

The experiments were confined to normal adults between the ages of 25 and 45. $CHCl_3$ was inhaled from a piece of lint, cut into a certain shape, and formed into a half cone over the nose and mouth. The amount was measured by drops out of a drop-bottle.

§ 15. *The introduction of "new conditions."*—In the course of unconsciousness (beginning with contracted pupil and normal colour of the blood) duskiness occurred, but under different circumstances. Ordinarily its appearance was late, and its progress was gradual. But in some instances it appeared early, and its rate of increase was comparatively rapid. Now there was a tendency towards uniformity in the progress of the phenomena in examples of the former group—viz., in the equally gradual increase in dilatation of the pupil and discoloration of the blood. But there was none in the latter. For amongst its members the pupil was found to have presented different characteristics: thus, in one sub-group the pupil underwent a gradual, in the other a rapid, dilatation. Inasmuch as there was manifest evidence of more or less obstruction to the action of the respiratory machine, in some instances where the large pupil existed, the source of the obstruction—viz., the displacement backwards of the base of the tongue—was removed. The procedure was not followed by the same results in all instances. In some the action of the respiratory machine was immediately and considerably improved, the degree of duskiness immediately and con-

siderably reduced, and the large pupil rapidly became small. In others, the improvement in the action of the respiratory machine and in the colour of the complexion was, at first, slight. The size of the pupil was reduced, but the degree of reduction was small. Afterwards improvement under the condition of the normally patent air-way gradually progressed, until what was then considered to be the "normal" state was reached. During the period of the induction of unconsciousness by the modified method, duskiness, when it appeared, was generally a late phenomenon. But occasionally it appeared early, and was always followed by muscle-phenomena. As the base of the tongue became displaced backwards during unconsciousness, it might conceivably become so during the stage of induction. When muscle-phenomena subsequently occurred as early phenomena, means were therefore taken to ensure the normal position of the base of the tongue. But they persisted and progressed, though the agent, which had been associated in thought with their causation, was known not to be in operation. The failure to explain these occasional occurrences led to a further consideration of the subject in the abstract.

Displacement of the base of the tongue is

one kind of mechanical obstruction in the air-way. Mechanical obstruction is capable of inducing duskiness. The question arose, "Are there any other kinds of obstruction present besides the displaced base of the tongue"? An examination of the air-way was thenceforward made when early duskiness appeared, and some obstruction in the nose — nasal stenosis —or in the pharynx — moderate amount of adenoid growths—were invariably found to be present.

A high proportion of $CHCl_3$ in a $CHCl_3$-air atmosphere is associated with the early occurrence of duskiness. When the proportion is reduced it is associated, 1, with the late appearance of duskiness when the air-way is normal; and, 2, with its early appearance when the air-way is abnormal. There is, therefore, an excess of $CHCl_3$ present in the air-way when duskiness is an early phenomenon, and this excess may be absolute or relative. Absolute excess is avoided by limiting the amount of $CHCl_3$. How is it possible to avoid a relative excess?

The mechanical obstruction is initial and permanent. To some extent its influence is counteracted by separating the lips. But even when the abnormal air-way is rendered as favourable as it can be, early duskiness supervenes, and is

followed by muscle-phenomena. The question of their causation appears to be apparently complicated by the fact that after the disappearance of the muscle-phenomena the maximum $CHCl_3$-air atmosphere is breathed without any difficulty, and accompanied by a less degree of duskiness than that which is associated with the early stages of the administration. For during induction the proportion of $CHCl_3$, though increasing, does not as yet reach the maximum. The apparent difficulty, however, led to the solution of the problem. If the maximum atmoshpere is breathed without difficulty during unconsciousness, what is the condition that determines the difficulty associated with it when it is breathed during the transitionary stage between consciousness and unconsciousness?

The analysis of the data which enter into the solution is as follows. An abnormal atmosphere is breathed through an abnormal air-way, and is associated with complication. But the same abnormal atmosphere is breathed through a normal air-way without complication. In both the same method is used—viz., the modified. It is characterised by the gradual introduction of $CHCl_3$ up to the maximum in the $CHCl_3$-air atmosphere breathed. They both have the same

maximum, and both are capable of breathing it without complication during unconsciousness. But in one, complication is presented during the transition from consciousness to unconsciousness. The datum, then, which is associated in causal relationship with the occurrence of complication, is the rate of increase of $CHCl_3$ in the $CHCl_3$-air atmosphere. It may not be a gradual but a degree of rapid increase—*i.e.*, relatively to the abnormal condition of the air-way.

An initial analysis of the air-way was thereafter instituted, and whenever respiratory obstruction was detected, the modified method was adapted so as to meet the requirements of the abnormal condition—*i.e.*, the rate of increase was reduced from the normal. After the experience of some difficulty, arising from the fact that different degrees of reduction were necessary for different degrees of obstruction (the higher degrees of which required a proportionately slower rate, and the lower ones only a slight change from the normal), the object was achieved of inducing anæsthesia, under the abnormal condition of respiratory obstruction, without the antecedent occurrence of duskiness and muscle-phenomena. And with their disappearance in these exceptional instances, muscle-

phenomena—purposive movements (struggling) and muscle-rigidity—disappeared altogether.

One source of perplexity was thus removed, but many others remained. And the following one became the next object of investigation. With the same amount of $CHCl_3$, administered by the modified method (and without the occurrence of complication), the degree of unconsciousness induced in different cases was found not to be the same. Thus, in one example, the pupil is normally contracted, and the colour of the arterial blood is normal. In another the pupil is more or less dilated, and the colour of the blood is more or less dark (the condition of the air-way being normal in both examples). What is the explanation of this difference in degree of results, associated with the same degree of $CHCl_3$-action?

If, in the case of the dilated pupil, the maximum amount is reduced, a diminution in size follows. If the amount of $CHCl_3$ is progressively reduced, the time will come when the pupil is normally contracted. And it was also observed that the return of the dilated pupil to the normal is accompanied by that of the abnormal colour of the blood to the normal. The variations in the size of the pupil and of the colour of the blood are correlated—*i.e.*,

a small reduction in the size of the pupil is associated with a small alteration in abnormal colour of the blood, a large reduction with a large alteration, until the pupil is normally contracted, when the colour of the blood is normal. If, therefore, the normal contraction of the pupil be taken tentatively as the measure of the anæsthetic degree of $CHCl_3$-action, the degree of dilatation will become the measure of the degree of over-action. And here it is necessary, in order to avoid misconception, to keep in view the limitations imposed upon this part of the investigation—viz., the presence of the normal respiratory machine, and the absence of a complicatory cause.

In the case under consideration let us suppose that a reduction from $^{a}6$ to $^{a}3$ drop $CHCl_3$-air atmosphere has to be made before the pupil reaches the condition of normal contraction. A 3-drop atmosphere will then represent the degree of the over-action of $CHCl_3$—*i.e.*, the amount in excess of that which is needed for the purposes of surgical operations. But a maximum proportion of 6 drops is required by the second of these two examples. Consequently, the maximum proportion is thus shown to be an inconstant factor. The conclusion, then, inevitably follows that the same $CHCl_3$-

air atmosphere, which is normal for one of the above examples, is abnormal for the other. Now, when the degree of action of a cause is kept constant, but the results associated with it vary in different examples, the source of the variation is to be found in a difference in the condition of the part affected. It remains, therefore, to isolate this part, the variant condition of which determines the maximum proportion for each individual case.

Respiratory obstruction (excluding extreme instances of it, associated with initial duskiness) has been shown not to exercise any influence on the maximum amount, but only to affect the rate of increase of $CHCl_3$ up to the maximum, in the $CHCl_3$-air atmosphere.

In order, then, to its elucidation, we have, up to the present stage of the inquiry, the following data: 1, The blood is the first tissue upon which $CHCl_3$ acts; 2, the same $CHCl_3$-air atmosphere is followed by different degrees of results in different individuals; 3, the constant action of the same $CHCl_3$-air atmosphere in the same individual is associated with a gradual but progressive increase in the degree of results. The notion of reducing the amount of $CHCl_3$ in the course of the state of unconsciousness, though it was entertained, had not as yet been

applied in practice. The occasion is now presented for considering it in the abstract with a view to its application.

The set of phenomena occurring in the progress of constant $CHCl_3$-action are similar to that which is associated with its initial over-action. The various degrees of over-action can be reduced to the normal immediately after the onset of unconsciousness. If the proportion of $CHCl_3$ is reduced when the pupil becomes dilated, after the antecedent condition of normal contraction, will it contract again?

The experiment of reducing the amount of $CHCl_3$ in the course of unconsciousness was conducted at the beginning on a limited scale, and the reason for this was the danger which was very generally believed to be associated with the return to consciousness. Thus small reductions were tentatively made. These were universally followed by the same variations which had occurred when the experiment was applied to the commencement of the unconscious state. In a few instances the second stage of returning consciousness was unintentionally reached. The deviation from the normal course originated in faulty administration. But no unfavourable result was observed to accompany it,—a circumstance which led,

1, to increasing confidence in the use of the contracted pupil, and, 2, to diminishing trust in the belief that returning consciousness is necessarily prejudicial to the patient's welfare.

By this means the average size of the pupil during the stage of unconsciousness was diminished. During the investigation of the gradual and progressive dilatation of the pupil, it was noted that when the amount was comparatively large—*e.g.*, 10 drops—the tendency was manifested very early, within 2′, whereas when the amount was smaller—*e.g.*, 6 drops—the manifestation of the tendency was delayed—*i.e.*, increase in the degree of dilatation appeared after an interval of 8′. The same feature, affecting the diminishment of the dilated pupil, appeared in the present series of experiments. When a reduction of the amount of $CHCl_3$ was made, a diminution in the size of the pupil followed, not immediately, but after a short interval. On the continuation of the reduced degree of $CHCl_3$-action, the pupil did not at once redilate, but it remained of the same size, viz., that to which it had been reduced, for a varying period, at the end of which it again began to dilate. And this period of comparative stability was found to have a relationship to the degree of $CHCl_3$-action. Thus, when the reduction was from 6 to 5 drops,

the interval was found to be on the average 5′; from 5 to 4 drops, 7′; from 3 to 2 drops, it was extended to 20′. A system was then devised which had for its object the progressive reduction in the amount of $CHCl_3$ during the course of its administration. And eventually it was perfected so as to maintain the pupil in the condition of normal contraction during the whole period of unconsciousness. As the result of this series of experiments, the following law was formulated: in the course of $CHCl_3$-action, maintained at the same degree, and associated with unconsciousness, the resistance of one (or more) of the parts upon which it acts progressively diminishes.

The normal course of $CHCl_3$-action had thus been isolated. And instead of being associated with any disadvantage to the severer forms of surgical operation, it was found to possess these two advantages in their favour. First, it allowed of the study of the occasional phenomena of respiratory and pulse-failure in their entirety. Secondly, it prevented opposition to the progress of natural complications—*i.e.*, it removed the so-called crisis, which formed the starting-point of the $CHCl_3$-hypothesis.

But the normal course of $CHCl_3$-action had not been isolated in all instances of the in-

duction-period. It appeared in a proportion only of a group of cases which were selected. When no discrimination was made, it was found that, with the inclusion of the young, of the old, and of those adults who presented variations from the normal, this proportion became smaller. Further, the attempt at the reduction of the initial dilated pupil of unconsciousness, which had been invariably successful in the former, was opposed in the latter. Out of 2000 successive cases, the pupil, which was fully dilated, resisted contraction in 3 per cent of them. (But on these occasions it invariably remained "sensitive" to light. When $CHCl_3$ was discontinued, it underwent a degree of contraction, but re-dilated on the resumption of the administration.) A practical difficulty arose when the usual guide to normal $CHCl_3$-action was unavailable. It was met by maintaining the normal colour of the arterial blood, unconsciousness having been induced; determined by the occurrence of automatic respiration, the colour of the blood is observed to be more or less dark, and the pupil more or less dilated. Generally, as has been already demonstrated, there is a direct proportion between variation in size of the pupil and variation of the colour of the blood—the

blood becoming less dark as the pupil becomes smaller. (In the exceptional cases there is a disproportion between these phenomena.) Instead, therefore, of the variation in the size of the pupil, the variation of the colour of the blood is, on these occasions, taken as the guide to the anæsthetic degree of $CHCl_3$-action. The dark colour of the arterial blood is gradually replaced by the normal, through successive reductions of the proportion of $CHCl_3$. The amount which coincided with the appearance of normal colour of the blood was then regarded as the anæsthetic amount. Having thus determined the necessary datum—viz., the lowest amount of $CHCl_3$ associated with unconsciousness in each case—the administration was continued on the plan above-mentioned. Unconsciousness was thus maintained, and with it the normal colour of the blood. From these exceptional instances of the sensitive dilated pupil, the inference is drawn that the relationship between $CHCl_3$-action and the blood is more intimate than that between $CHCl_3$-action and the pupil.

In this series of 2000 cases, observations were made of the frequency of the pulse, and of the acceleration of respiration. And in order to obviate an error which had appeared in previous

records—viz., the influence of emotion on the pulse—the observations were taken, not immediately after the appearance of the normally contracted pupil, but at the end of a period of 5′. For the results of emotion on the pulse do not cease on the suspension of the emotional function. It is therefore essential that these should have completely disappeared if a pure $CHCl_3$-result is to be obtained. Under these circumstances, the average pulse was found to be in the male 73, in the female 75; and the respiration in both 28. But further investigation showed that these averages do not remain constant during the whole period of anæsthesia. There was in both a tendency towards variation, which first appeared in increased acceleration of the respiration, and subsequently in an addition to the frequency of the pulse. And the following relationship was observed to exist between them—viz., the pulse-variation is directly proportioned to the respiratory-variation.

Besides these, further observations were made on nerve- and muscle-stimulation, which led to the following conclusions. 1, In the early stage of anæsthesia, nerve-stimulation is followed by immediate and vigorous muscle-contraction; in the later stages, by immediate but faint contrac-

tion. 2, In the progress of anæsthesia, the muscles become less sensitive to the influence of direct stimulation: their degree of relaxation progressively increases.

With the use of the anæsthetic degree of $CHCl_3$-action, it was very soon remarked that the return to consciousness was rapid, as compared with the prolonged period which formerly obtained when large amounts had been administered. In normal cases the return is effected within a period of 5′, following upon the discontinuance of $CHCl_3$. And the records which were taken in order to test the value of the so-called "after-effects" showed that lassitude and headache had to a large extent disappeared, and that the instances of sickness had been reduced to a very small group. The reason of this remarkable change is not very far to seek. The use of large amounts of $CHCl_3$ is associated with an abnormal state of the arterial blood. It is imperfectly oxygenated, and it contains an excess of CO_2. This condition of the arterial blood is opposed to normal nutrition. The brain, the stomach, and the muscles all suffer from impairment of their ordinary food-supply, from the consequences of which they have subsequently to recover.

In the case of anæsthesia, there is no impairment of nutrition—at least, there is no apparent impairment if $CHCl_3$-action be excluded (and on the supposition that it is injurious, the degree of its result is reduced to a minimum), for the blood is efficiently oxygenated, and preserves its normal colour. The $+CO_2$ state of the arterial blood (or $-OXy$) is therefore the intermediate factor, which explains the occurrence of after-results.

The ordinary phenomena of the action of $CHCl_3$ having been isolated, and proof afforded that they vary in degree according to the degree of $CHCl_3$-action, the field of investigation became open to the study of its assumed extraordinary action. It became obvious, at the outset, that the inquiry could not be confined to the mere occurrence of respiratory or pulse-failure; for though either is a prominent phenomenon, it does not occur "alone," but is accompanied by other phenomena, some one of which may possibly have an important influence, either in determining the source of the abnormality, or else in leading to the removal of "obstacle" in the way of recovery. The inquiry, then, is to be not partial, but comprehensive. All the phenomena are to be included in order to avoid the possible error

of leaving out the most important one. This leads to their logical treatment.

§ 16. *The logical treatment of phenomena occurring during $CHCl_3$-action.*—When a phenomenon appears in a component part of a complex system, it is followed by the appearance of other phenomena in, 1, the same system, and, 2, other systems which are related to it. Philosophically, cause and effect are one and the same. What, however, we have to deal with is the result, for a cause acts upon some part, the condition of which may be, but is not necessarily, constant. Now, it is this tendency towards inconstancy of conditions that proves so perplexing a factor in the investigation of the action of $CHCl_3$. Cause and direct result are simultaneous. A distinction, however, is to be made in the case of vital tissues; for these present a greater or less degree of resistance to the action of agents which are injurious to them, according to their actual condition at the time when they are affected. The power which enables them to do this is one of self-preservation. Thus, though the action of an agent prejudicial to their wellbeing is necessarily followed by its effect, yet the degree of result will be determined by the amount of resistance that is opposed to the agent, and its full effect will only

be manifested in the result upon them after all their resistance is overcome. But by reason of the variety of the parts involved, there is a distinct interval between the operation of the cause and the appearance of the phenomena which are ordinarily associated with its action. In these the phenomena are not the direct, but the indirect, results of the cause. For example, a moderate degree of stimulation of the vaso-motor centre and fall of blood-pressure are simultaneous, and the direct result is there manifested to the sense. But if, in the course of normal anæsthesia, complete obstruction of the air-way, by artificially displacing backwards the base of the tongue, be maintained for a period of 5″, there is a distinct interval between the operation of the cause and the appearance of, 1, variation in the character of the respiratory movements, and, 2, a slight degree of duskiness. The effect of complete mechanical obstruction is upon the air in the air-way below the seat of obstruction. There is sufficient oxygen at first for the requirements of normal aeration. After an interval which is necessarily very short, the amount of oxygen becomes insufficient for that purpose, for the inspiratory movements do not replace the oxygen which has been absorbed by a fresh supply. There

is, consequently, a temporary impairment of the function of aeration. The phenomena immediately dependent upon this impairment are, 1, variation in the character of the action of the respiratory machine, and, 2, duskiness. Presenting initial slight degrees of intensity, corresponding to the slight degree of impairment of aeration, they subsequently become increased as the degree of impairment increases. If, now, the ultimate cause, mechanical obstruction, is put out of operation, the impaired function of aeration does not at once become normal, for the reason that impairment of aeration is the cause of physiologic pulmonic congestion. Normal aeration implies, 1, normal alveolar circulation, and, 2, normal supply of oxygen. Aeration becomes normal when the alveolar circulation is rendered normal—*i.e.*, when pulmonic congestion disappears. The time necessary for the reduction of pulmonic congestion varies according to the degree of its intensity.

Now the condition of the alveolar contents, which are primarily affected by mechanical obstruction, are not capable of being seen. It has, in consequence, to be inferred from the results which it produces. Diminution of oxygen in the alveoli has two spheres of action. In the one it produces distension of the pulmonic

artery; in the other, discoloration of the blood. But slight degrees of intensity of the latter are capable of being detected earlier than corresponding degrees of intensity of the former. Hence the importance in practice of observing faint degrees of discoloration of the blood. For it points at once to the action of an adverse cause, and leads to the immediate removal of it before its results become unduly intense.

§ 17. *The same phenomenon may have different causes.*—A fall in blood-pressure is caused by, 1, stimulation of the vaso-motor centre; 2, cardiac syncope. In the human, and under the circumstances affecting the administration of $CHCl_3$ for the purposes of surgical operations, the stimulation of the vaso-motor centre is always reflex; some branch or local centre of the sympathetic nervous system is stimulated, and the stimulus is conveyed to the vaso-motor centre. Cardiac syncope may be primary or secondary. Primary syncope may be due either to some inherent defect in the heart or to the action of some agent upon it. In the present inquiry there is only one such possible agent, and that is $CHCl_3$, which is assumed to be absorbed into and circulate in the blood. Secondary syncope is the result of cardiac exhaustion, following upon distension of the right ventricle.

Arrest of the action of the respiratory machine may be caused by—1, mechanical obstruction, of which it is a late phenomenon; 2, physical obstruction, resulting from a respiratory overdose of $CHCl_3$; 3, exhaustion of the muscles of respiration; 4, functional arrest of the action of the respiratory centre; 5, voluntary arrest of the action of that centre (its occurrence being restricted to the transitional period between consciousness and unconsciousness); and 6, the assumed direct action of some agent upon the respiratory centre. As in the case of the heart, the inquiry is restricted to $CHCl_3$. Dilatation of the pupil is associated with—1, fall of blood-pressure, induced either rapidly or suddenly; 2, duskiness in certain circumstances. The dilated pupil, when associated with duskiness, may be, 1, sensitive, or, 2, more or less sluggish to the sudden application of light.

Muscle-phenomena may be caused by—1, volition; 2, stimulation of the spinal centres; and 3, $+CO_2$ (or $-OXy$) condition of the arterial blood. Two data are requisite in the latter case. The degree of the $+CO_2$ condition must be sufficiently intense, and it must be rapidly induced. Thus any phenomenon appearing in the course of $CHCl_3$-action is not

necessarily the result of it. Before a causal nexus can be established between $CHCl_3$-action and the phenomenon, it is requisite to exclude the operancy of all other possible agents. And afterwards the nature of the association, whether direct or indirect, remains to be determined.

§ 18. *The mode of onset of a phenomenon.*—Each mode of onset has its particular characteristics, with which observation, applied continuously from the beginning of the abnormality, makes us familiar. Two modes only were formerly differentiated—viz., the rapid and sudden. Thus the pulse failed suddenly or rapidly. The arrest of the action of the respiratory machine was either sudden or rapid. These, however, do not include all the modes of onset of those phenomena. For example, there is the gradual arrest of respiratory movements, of which there are two kinds. And further, the original analysis was imperfect, inasmuch as it did not differentiate between the different kinds of rapid arrest, each of which is characterised by its particular mode.

It does not suffice, therefore, for the purpose of correct inference, to assert that either the pulse or the respiratory machine fails rapidly or suddenly. For the "condition" of the respiratory muscles varies at the onset of arrest,

and, in the instance of rapid arrest, is a determinant of the degree of the rapidity with which it takes place. The condition of the respiratory muscles which characterises the mode of onset of rapid arrest is the degree of their tone. Rapid arrest may be associated with—1, antecedent increased activity of the respiratory machine (*i.e.*, a complication occurs during this increased activity, leading to rapid arrest); 2, inhibited respiration; and 3, obstructed respiration, in which the proximate cause of arrest is either due to increase in the initial source of obstruction—viz., the backward displacement of the base of the tongue—or the intervention of a collateral complication.

In the case of sudden arrest of the action of the respiratory machine — formerly called respiratory failure — it is necessary to state whether it occurs at the end of expiration or during inspiration, for the incidence of its occurrence may have a bearing on its causation. The state of the respiratory machine may be normal or abnormal when it occurs, but in either case it does not exert any influence on the mode of onset, for the reason that all forms of sudden respiratory arrest derive from suspension of the function of the respiratory centre. The abnormal state of the respiratory machine,

however, is of practical importance in that it masks the simple character of the complication, and determines the occurrence of arrest at some stage during the act of inspiration, before its completion. There are differences in the degree of rapidity of pulse-disappearance. They are determined by the different conditions under which they occur. But sudden disappearances of the pulse present no differentiating characters. Consequently, they provide, in themselves, no means of arriving at their causation. In order to distinguish between their causes, the means of differentiation are to be sought elsewhere, and they are found in the different attitudes of the respiratory machine accompanying them.

§ 19. *The phenomena concerned in the solution of the $CHCl_3$-problem.*—These include variations in—1, the action of the respiratory machine; 2, the circulatory system; 3, the pupil; 4, the muscular system; and 5, the blood.

The principal phenomena are generally taken to be those occurring in the two vital systems. The remaining ones are generally regarded as subsidiary, but are of value in that they supply the means of differentiating between degrees of action, both of $CHCl_3$ and complicatory agents. Muscle-relaxation may, however, under favour-

able circumstances, occasion impairment of the function of aeration through the backward displacement of the base of the tongue, which, if not counteracted, influences adversely those $CHCl_3$-results which it is the object of investigation to isolate—viz., the increase in the frequency of respiration and the condition of the pulse. The two prominent phenomena, which formerly occupied the whole field of inquiry, being arrest of respiration and disappearance of the pulse, the question arises, "How are they caused?" And the same simple explanation might be given now as was then—viz., that there is a common cause of all instances of respiratory arrest, and it is paralysis of the respiratory centre, and a common cause of all instances of pulse-disappearance, and it is cardiac depression. But such a view is, on the merest examination, found to be inadequate. For the problem of the causation of respiratory arrest is not simple, but highly intricate; the intricacy appearing in the complex structure of the respiratory machine, in any one of the components of which abnormality may occur and lead to the arrest of its action. Now, the sources of disturbance are many, including the action of $CHCl_3$. It is conceivable, therefore, that the same component may be affected by two agents,

of which $CHCl_3$ is one. And it is also conceivable that one component may be affected by $CHCl_3$, while another one may be simultaneously affected by a collateral agent. The need of analysis thus becomes imperative. For before we can proceed to the conclusion that $CHCl_3$ is the cause of respiratory arrest, it is requisite to prove the absence of every other cause which may produce it. When it is demonstrated that $CHCl_3$ is the sole, or at any rate the chief, factor in the causation of respiratory arrest, as it may be in two different ways, it then becomes pertinent to inquire, "How does $CHCl_3$ act so as to produce this result?"

The same complexity involves the circulatory system. The disappearance of the pulse may be caused by an abnormal condition of the heart. It may also be caused by an abnormal condition of the vaso-motor centre. Before we conclude that the origin of the complication is in the heart, it is necessary to exclude the influence of the vaso-motor centre. But instances occur in which respiratory movements become "shallow," but do not cease, and the pulse becomes reduced in strength, but does not disappear. And they recover. What relationship have these "minor" phenomena respectively to the "major" phenomena of respiratory arrest

and pulse-disappearance? The relationship is one of degree. Knowledge of the latter is therefore acquired from the study of the former, which is now rendered simple by the use of the anæsthetic degree of $CHCl_3$-action. Thus, the minor phenomena become the key to the solution of the $CHCl_3$-problem. For it is by their uncomplicated progress during the administration of $CHCl_3$ that the operation of causes, acting independently of $CHCl_3$, is demonstrated.

§ 20. *Sets of Phenomena.*—Phenomena do not occur "singly" during $CHCl_3$-action. The notion that they do so leads to the exclusion of accompanying phenomena. Amongst these, conceivably, may be that one which points to the cause of the complication. For if a single phenomenon, which in reality is but one of a set of phenomena, be, in idea, removed from its surroundings, and regarded as the whole of the result or complication, and inferences are drawn from it, there is a chance of error appearing in the conclusion. The chance depends on whether the selected phenomenon is or is not fundamental. Thus pallor occurs in company with respiratory inhibition and dilatation of the pupil. It is taken as the starting-point of inference. It is inferred to be the result of $CHCl_3$-action on the heart. There is a bias in

favour of this explanation, deriving from the original hypothesis. But in reality pallor is not the fundamental phenomenon. It is, on this occasion, of secondary importance. Hence, the inference drawn from it will be erroneous.

To avoid such error, it is necessary to include, 1, all the phenomena; and, 2, the order in which they appear. Thus correct records are obtained, founded on complete and accurate observation.

There are two main groups of phenomena occurring in the course of $CHCl_3$-action. One is characterised by inefficient aeration; the other by variations appearing in the respiratory and circulatory systems, independent of inefficient aeration, but sometimes accompanied by it.

I. The phenomena associated with inefficient aeration are: duskiness (discoloration of the arterial blood), venous distension, increased activity of the respiratory machine, increased frequency of respiration, increase of blood-pressure, and diminution of pulse-frequency. They all appear simultaneously, and when they undergo variations, either of increase or of diminution, the degrees of variations are in direct proportion to each other.

The inconstant phenomenon associated with duskiness is the pupil. It may remain normally contracted while the constant phenomena are

increasing in degree; or it may present a progressive increase of dilatation, the degree of increase being in direct proportion to that of the constant phenomena. In the former, contraction is only maintained up to a certain stage in their progress, characterised by respiratory-interruption, when the pupil dilates rapidly and fully. In the latter, as the degree of dilatation increases, the sensitiveness of the pupil to light diminishes.

The value of the pupil is thus established as the means of differentiating between two classes of duskiness. And its actual condition leads to the detection of the cause in any given simple instance of duskiness appearing in the course of $CHCl_3$-action. If the pupil is normally contracted, the cause is mechanical obstruction; if, on the other hand, the pupil is dilated and less than normally sensitive to light, the cause is the narcotic action of $CHCl_3$.

II. In the second group, a variation of one of the parts of the respiratory system—*e.g.*, complete mechanical obstruction—is followed by variations of the frequency and tension of the pulse. These do not appear immediately after respiratory obstruction, for the reason that the latter is not coincident with immediate defective aeration. A small interval elapses before they

become manifested; and in their progress the degree of their intensity is increased. In like manner, a variation of the circulatory system—*e.g.*, primary cardiac syncope—is followed by a variation of the respiratory machine, the action of which, at first inappreciably altered, afterwards gradually declines. In these instances there is a clear interval between the occurrence of variation of one system and the appearance of a marked degree of variation of the other. The interval is less, and may be ignored altogether if continuous observation be not maintained between functional arrest of the action of the respiratory centre and rapid disappearance of the pulse, and also between sudden disappearance of the pulse and rapid decline of respiratory movements.

But there are some instances of variations of the respiratory and circulatory systems which present no such interval, capable of being perceived by the sense either of touch or sight. Thus they are apparently simultaneous in their appearance. But it is necessary to effect their separation in the order of time in which they occur, for the purpose of isolating the phenomenon which points to the cause of the complication. And here inference comes to our aid. In anæsthesia there are only two com-

binations, the members of which require to be analysed into antecedent and consequent. They are, 1, pallor and respiratory acceleration; and, 2, respiratory inhibition and pallor. When pallor and respiratory acceleration occur apparently simultaneously, it is inferred that pallor is the antecedent and respiratory acceleration the consequent, because it is a physiological axiom that stimulation of the vaso-motor centre—the cause of pallor—is followed by secondary stimulation of the respiratory centre—the cause of respiratory acceleration. And so with respect to the simultaneous appearance of respiratory inhibition and pallor. It is known that stomachic inhibition of the respiratory centre is followed by secondary stimulation of the vaso-motor centre. Whenever, therefore, respiratory inhibition and pallor are associated, the former is taken to be the antecedent, and the latter the consequent. The field of investigation then becomes limited to the isolation of, 1, the cause of stimulation of the vaso-motor centre; and, 2, the cause of inhibition of the respiratory centre.

These variations of the circulatory and respiratory systems are clearly defined when the conditions are normal—*i.e.*, $CHCl_3$-action limited to the degree of anæsthesia, and the air-way

normally patent. They may, however, occur under abnormal conditions. These include—1, some degree of respiratory obstruction; 2, temporary respiratory overdose of $CHCl_3$; and 3, some degree of excessive $CHCl_3$-action, either of which may act singly or they may co-operate in any combination. As they are in themselves complications, it follows that two or more complications may coexist. Thus there may be—1, some degree of excessive $CHCl_3$-action; 2, mechanical obstruction to the air-way; and 3, stimulation of the vaso-motor centre. Out of the complex results proceeding from this combination of causes, some part is due to $CHCl_3$. But what is that part? The three chief phenomena to be explained are—1, the disappearance of the pulse; 2, the rapid decline, ending in the arrest of respiratory movements; and 3, the dilatation of the pupil, which exists before the pulse disappears. The part ascribed to $CHCl_3$ may be confined to the disappearance of the pulse. And to explain it, $CHCl_3$ is assumed to act upon the heart. But in the first place, the disappearance of the pulse does not necessarily signify weakness of cardiac action; and in the second, a collateral cause of the disappearance of the pulse is ignored. Such a combination of causes, therefore, in-

cludes the possibility of ascribing to $CHCl_3$ a result which does not belong to it. But suppose that $CHCl_3$ acts in the way assumed. The conclusion still remains a partial but not a complete explanation of all the data under consideration. For the dilatation of the pupil, which antecedes the disappearance of the pulse in this instance, is not an invariable antecedent in all instances. To complete the investigation, it is therefore necessary to make the following inquiries: 1, what is the cause of the dilatation of the pupil? and 2, what is the relationship of this cause to $CHCl_3$?

§ 21. *The fundamental Phenomenon.*—The sets of phenomena which may appear during the course of $CHCl_3$-administration are called "states." The inquiry into the nature of $CHCl_3$-action consists of the logical treatment of these states and not of arbitrarily associating single phenomena with that action. An important step is thereby made towards its true solution.

The "state" is normal or abnormal. Abnormal states differ; their differentiating characters are determined by the complicatory causes which produce them.

When a change occurs in a state, the phenomenon which appears first is called primary or fundamental, because it is nearest the cause

producing the change. The change may be associated with a variation of the degree of $CHCl_3$-action, from a degree less than the anæsthetic to the state of anæsthesia, or from anæsthesia to some degree of narcosis, or *vice versa*. Or it may be associated with the operation of a cause independent or dependent on $CHCl_3$-action. In the latter case, the collateral cause may operate during any degree of $CHCl_3$-action, unless means are used to limit the degree of its action, and maintain it at that limited degree. Thus a complicatory cause may appear during, 1, one of the stages in the induction of unconsciousness; 2, anæsthesia; or 3, narcosis.

A cause produces its effect on some condition of some part of the organism. And it is essential to bear in mind, but the more particularly where vital tissues are concerned, that the separation between cause and effect was a trick of the imagination, performed in order to subserve the function of reasoning. In nature, cause and effect are simultaneous and identical. As soon as a cause begins to operate, its effect is at once produced. But what we see is not this effect simply. It is the effect modified by the condition of the part on which the cause acts. The change produced in this part is

called the result. And it is obvious that we shall fall into error if we mistake results for effects.

But all results do not appear to us, for the reason that the organs in which they occur are hidden from view — *e.g.*, changes in the condition of the lungs and heart. When the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere is raised so as to cause impairment of aeration, the results are — 1, discoloration of the arterial blood; 2, reduced capacity of the left ventricle; 3, distension of the pulmonic artery; 4, distension of the right ventricle; 5, diminution of frequency and increased tension of pulse; and 6, distension of the venous system.

The discoloration of the arterial blood and the distension of the pulmonic artery, generally described as pulmonic congestion, are taken to be the first to appear, and are therefore called fundamental results. (For a cause may have more than one sphere in which it operates. But it can only have one effect in each of them.) The other results are termed indirect or remote, because they are in thought farther away from the cause on which they are dependent. But in the natural course of affairs, any diminution of the amount of blood supplied to the left

ventricle is at once associated with a corresponding reduction of its capacity. There is no interval between these results. But before it is possible that the left ventricle should automatically become reduced in size, it is necessary that its supply should be diminished, and this can only be effected, under the circumstances, by reducing the rate of the alveolar circulation, which again can only be caused by diminishing the supply of the agent upon which it depends—viz., oxygen. The isolation of these fundamental results is thus perceived to be determined by thought.

Pulmonic congestion is associated with, 1, increased tension and diminished frequency of the pulse; and 2, venous distension. Discoloration of the arterial blood is associated with duskiness of the complexion. (On some occasions it is possible to observe this primary result *in situ*—viz., when the operation-wound is exposed to the view of the chloroformist.) Both these results depend upon a physical cause, and one of them, pulmonic congestion, causes a simple physical result—viz., distension of the right ventricle—which, in its turn, becomes the cause of venous distension. Its maximum degree, however, is not reached suddenly, because it is induced indirectly; but it

may be rapidly. In this respect physical differs from physiological causation—viz., stimulation of nerve-centres. When a nerve-centre is stimulated, its maximum result is immediately induced, and corresponds to the degree of stimulation. And in the case of the vaso-motor-centre, the initial degree of stimulation may suffice to cause the sudden disappearance of the pulse. On the other hand, pulmonic congestion has to reach a certain degree of intensity, and to be maintained at that degree for a certain time before it is followed by the disappearance of the pulse. In that contingency there is a period of increased pulse-tension and diminished pulse-frequency, which is antecedent to its disappearance. This period is determined, 1, by the degree of pulmonic congestion; and, 2, the duration of its maintenance. In these circumstances the disappearance of the pulse is invariably rapid.

The primary or fundamental phenomenon points to the causation of the complication. Where there is but one cause of the same result—*e.g.*, impairment of the function of aeration causing duskiness—no difficulty is presented. But where there are two or more causes of the same result, as, for example, in the case of a fall of blood-pressure, difficulty

appears in the isolation of the particular cause. It is here that the value of concomitant phenomena becomes evident. A change takes place in the state of the patient during $CHCl_3$-administration. The origin of the change is in the vascular system, and it is a sudden fall of blood-pressure. What is the particular cause of the fall? It may be either, 1, stimulation of the vaso-motor centre; or, 2, cardiac syncope. Differentiation between these causes is made by calling to our assistance the phenomena presented by the respiratory function. In one group of instances it is found that immediately upon sudden fall of blood-pressure, rapid decline of the action of the respiratory machine follows. In another, which comprises but few examples, the action of the respiratory machine continues unaffected at first by the fall of blood-pressure, and then gradually declines. Now, the rapid or gradual decline of the action of the respiratory machine aids us in isolating the particular cause in this way. The vaso-motor centre is in intimate relationship with the respiratory centre. A change in either is forthwith communicated to the other. Thus, where the vaso-motor centre undergoes a severe degree of stimulation, the respiratory centre is sympathetically affected by it, and its function rapidly

declines. But when the origin of the fall of blood-pressure is cardiac syncope, there is no necessity for the respiratory centre to undergo any change at all, for the simple reason that there is no immediate relationship between the function of the heart and that of the respiratory centre. The function of the centre continues, as long as the respiratory muscles are able to perform their duty, under the most unfavourable conditions—viz., cessation of their supply of blood. If this is not restored, their action, after the consumption of their reserve-power, subsequently declines, and declines gradually in accordance with the law of the gradual disappearance of muscle-vitality, when separated from its source.

The proximate cause of fall of blood-pressure being traced to the heart, the question which next presents itself for solution is, "What is the ultimate cause of cardiac syncope?"

There are two possibilities. I. The cause of syncope is inherent in the heart, and manifested in some kind of abnormality which is known to be associated with sudden failure of function. II. The cause of syncope is the action of $CHCl_3$ on the heart. The hypothesis that $CHCl_3$ directly influences cardiac function is based on two propositions: 1, $CHCl_3$ circulates

in the blood, and is carried to those parts of the organism for which it has "affinity"; 2, the occasional occurrence of cardiac syncope having a fatal termination.

In the example of severe stimulation of the vaso-motor centre, there is sudden fall of blood-pressure, and in order to meet the temporary disturbance in the vaso-motor system, the heart automatically reduces the power of its contractions. These may be reduced to a minimum. The reduced action of the heart is thus not a primary but merely a secondary result. If the conditions antecedent to the occurrence of the vaso-motor complication are normal, the return of the natural power of the heart's action is gradually effected by assisting the progress of a natural but abnormal function. The main mass of the blood is diverted into the portal system. Its way back to the main is through the alveolar circulation. It is obvious that the normal patency of the air-way is of the first importance, oxygenation being the means by which the blood is conducted from the right to the left ventricle.

Let us suppose that the conditions antecedent to the occurrence of fall of blood-pressure are not normal, and that pulmonic congestion is present with its invariable consequent, distension

of the right ventricle. Pulmonic congestion opposes an obstacle, greater or less according to its degree, to the passage of blood from the right to the left side of the heart. The supply of blood to the left ventricle, being the natural stimulant of ventricular contraction, is diminished, and it may be practically cut off. There is no inducement, therefore, for the heart to functionate in the latter contingency; but serious interruption to its functional activity is not necessarily fatal. It becomes so when the interruption is prolonged—*i.e.*, there is delay in the supply of blood to the left ventricle. In these circumstances, the tendency might be to regard the cessation of the cardiac function as primary, for, first, the pulse disappears before respiratory movements cease; and secondly, the heart does not respond to artificial stimulation. And the further inference that $CHCl_3$ is the cause of cardiac failure will strengthen belief in the hypothesis. But the foundations of all these inferential conclusions are not sound. The ultimate failure of the heart is not necessarily a primary result. It may be only a secondary one. The determining factor is the actual condition of the heart at the time of the disappearance of the pulse. In what way can this be demonstrated?

Let us suppose that instead of continuing the adverse surroundings of the heart, a procedure which will tend to its failure, some amelioration is at once effected in them, as by reducing the degree of pulmonic congestion, and thus favouring the passage of blood to the left ventricle. A change of conditions will thus be induced, determining the attitude of the heart. If its action has simply been reduced, it will gradually resume its power, provided that there is no interruption to the progressive diminution of the degree of pulmonic congestion, for upon this depends the gradual increase of the supply of blood to the left ventricle. If, on the other hand, the heart has ceased to beat, any remedy is obviously useless. But that conclusion cannot be reached in all instances with certainty. In doubtful instances the prudent course to pursue is to put into operation, immediately after the occurrence of "crisis," the means of treatment which has for its end-object the relief of an assumed embarrassed condition of the heart—viz., artificial respiration. For this is the only way to discover the factor which is unknown—viz., the actual condition of the heart.

Relief is to be immediately applied, for two reasons: 1, the reduced power of the heart is being exhausted by its effort to overcome the

obstacle opposed to it; 2, the degree of intensity of the obstacle is increased by the effort of the heart. Thus, the conditions after the occurrence of crisis do not remain the same, in the case of reduced cardiac action; consequently, if any undue delay takes place in the application of artificial respiration, the conditions may become so unfavourable that the remedy will be of no avail.

Danger is involved in mistaking secondary for primary results, when the inference drawn therefrom is made the basis of treatment. For example: the pulse disappears, followed by rapid arrest of respiratory movements. The cause of the complication is assumed to be cardiac failure: all the possible causes, and therefore, in some instances, the actual cause, being thus arbitrarily excluded, initial treatment is directed to the artificial stimulation of the heart. Artificial respiration is resorted to after the attempt to restore the cardiac function has proved unsuccessful. Now there is the probability, when the differentiating phenomena are ignored, that the cardiac result is not primary failure, but reduced action. As the consequence of delay, the conditions in this contingency will be adverse to the success of artificial respiration, or may be impossible for it.

§ 22. *Classification.*—The results associated with $CHCl_3$-action present a complete field for inductive investigation. The conditions of all the functions without prejudice in favour of any particular one associated with a given degree of $CHCl_3$-action being recorded, and used as a temporary standard, it is easy to determine the variations of those conditions accompanying variations of degree of action. Thus, with a given degree of $CHCl_3$-action, there is observed, 1, duskiness (some degree of); 2, increased activity of the respiratory machine (some degree of); 3, dilatation of the pupil (some degree of); and, 4, diminution of pulse-frequency (some degree of). If, now, the degree of action is increased up to a certain limit, it is perceived that all these phenomena present an increase of degree of intensity; if we reduce it, that they also undergo a reduction of degree. A comparison being instituted between the components of these different states, it is found that they are all directly proportioned to each other. If, again, comparison is made between the degree of variation of these phenomena and the degree of action, it is also found that they are in direct proportion to each other. If, lastly, $CHCl_3$-action be reduced to its lowest limit—*i.e*, anæsthesia—a set of phenomena will be obtained

which are now taken to represent its "standard" action. But the action of $CHCl_3$ being maintained at the same degree, it is observed that its results—viz., the set of phenomena comprising the state of anæsthesia—do not remain constant, but tend, after a period, to vary. The nature of the variation which thus occurs in the phenomena corresponds exactly to overaction of $CHCl_3$. A relative over-action is thereby induced—*i.e.*, the same degree of $CHCl_3$-action is eventually associated with an increased degree of intensity of results. In order to maintain normal $CHCl_3$ results—*i.e.*, the constant state of normal anæsthesia—it is necessary, therefore, to reduce the degree of action in accordance with, and after the manner determined by, the law of diminishing resistance.

The parts which are primarily affected by $CHCl_3$ in its different spheres of action are, 1, the respiratory machine; and, 2, the blood. But in the case of the latter a difficulty is presented. For, while there is no discoloration of the arterial blood in anæsthesia, there is in narcosis. And the difficulty resides in the fact that there is already a cause in operation which is known to produce discoloration. It is an atmosphere containing less than the normal proportion of oxygen, and it is necessarily

associated with the higher degrees of $CHCl_3$-action.

In determining the direct relationship of $CHCl_3$ to the blood, we have to exclude the influence of this factor.

The respiratory machine and the blood do not always present the same initial conditions. These are differentiated into normal and abnormal. And thus the relationship of $CHCl_3$ to abnormal conditions forms the centre of inquiry. An initial abnormal condition, unless isolated and rationally treated according to its particular requirements, introduces "irregularity" in results, and therefore perplexity in the solution of the $CHCl_3$-problem. When the initial conditions are normal, and the normal method of inducing and maintaining anæsthesia is applied to them, the results are normal. The conditions of the respiratory and circulatory systems and of the pupil are rendered constant. (More correctly, as constant as they can be made under the circumstances, for there is a tendency to variation of the frequency of the respiration and pulse in the later stages of anæsthesia, which, however, can be measured.) Variations occurring in them can be easily observed, records taken and collated.

The result of classification of the abnormal

states appearing during $CHCl_3$-anæsthesia is the formation of three principal groups, each of which has a characteristic phenomenon. They are—1, duskiness; 2, inhibited respiration; and 3, fall of blood-pressure. The latter is further subdivided into, 1, non-disappearance of the pulse; and 2, disappearance of the pulse. And the latter is further divided into two groups: 1, with simultaneous decline of the action of the respiratory machine; and 2, without immediate change of its action.

All these groups present typical examples. But though there is a fundamental resemblance between the examples of any one group, all of them are not exactly similar. The difference originates either in a variation of the degree of the abnormal phenomena, or in the appearance of new phenomena. Thus, the group of abnormalities, whose common factor is inhibited breathing, exhibits three different terminations. 1, The inhibition of the respiratory centre ceases after a longer or shorter interval; 2, in the course of inhibited respiration, arrest of the action of the respiratory machine takes place, followed immediately by the act of vomiting; 3, in the course of inhibited respiration, arrest of the action of the respiratory machine occurs during inspiration, but is not followed immed-

iately by the act of vomiting. This sub-group forms one of the sources of perplexity which invades the study of $CHCl_3$-action. For, however important the arrest of respiratory movements may be from the practical point, from the causal point it is here of secondary importance, being an incident in the performance of a natural function.

In the group of cases which present "duskiness" as their characteristic phenomenon, the pupil may be either normally contracted or more or less dilated. The cause of the dilatation is the relative over-action of $CHCl_3$. The degree of $CHCl_3$-action remaining the same, the conditions of the respiratory machine and of the blood become abnormal through the partial displacement of the base of the tongue. This abnormal set of conditions requires a less degree of $CHCl_3$-action. If no reduction is made, a relative overdose follows. The rate of increase of duskiness is accelerated, and the pupil gradually dilates with a tendency to the loss of its sensitiveness. The original complication—simple mechanical obstruction—thus becomes masked. This masking of complicatory phenomena by the relative over-action of $CHCl_3$ provides one of the sources of dissimilarity existing among examples of the same group.

And it is explained by the fact that the same proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere does not preserve the same relationship to all conditions of the respiratory machine and of the blood. The alteration in relationship proceeds from, 1, the negative action, and, 2, the physical action, of $CHCl_3$. For example, mechanical obstruction causes deficient oxygenation. The proportion of $CHCl_3$ is adjusted so as to maintain the deficiency (practically) at the same degree. Inhibition of the action of the respiratory machine is synonymous with its reduced power. $CHCl_3$-vapour being relatively heavy as compared with air, its weight is to be adjusted to the power which moves it. If this is not done, an accumulation of $CHCl_3$ in the air-way results—*i.e.*, a relative respiratory overdose. In such an instance no control is exercised over the physical action of $CHCl_3$. As the result of the combination of these two causes, more or less rapid (according to the degree of respiratory overdose), arrest of respiratory movements occurs. But stomachic inhibition of the respiratory centre may at any moment be converted into the functional arrest of its action, which is invariably sudden. There is the attempt at full inspiration antecedent to the act of vomiting. The abnormal contents of the

air-way are unfavourable to its completion, in that they oppose an obstacle to the entry of the requisite supply of air.

§ 23. *Causation.*—To each set of phenomena there is one cause. The primary or fundamental phenomenon points to it. If a single phenomenon be selected as the foundation of a generalisation—for example, all instances of arrest of respiratory movements depend upon paralysis of the respiratory centre,—because it is assumed that in one instance it is so—a fallacy is committed, inasmuch as there are other causes of arrest which, though in operation at the time, are not taken into consideration, and hence their influence is not excluded. But there is no proof alleged to show that, in any instance of the (temporary) disablement of the respiratory machine, the vitality of the respiratory centre is impaired. The origin of the fallacy is in the treatment of the selected phenomenon. It is taken to be fundamental, in all instances, whereas it may be the result of a secondary cause—*e.g.*, depression of the respiratory centre following upon severe primary stimulation of the vaso-motor—or an incident in the progress of a collateral one—viz., the abnormal action of the stomach. Each cause has only one mode of operating. But seeing that any one cause may

have two or more spheres of action in the human organism, it follows that it may have two or more modes of operating, but in different spheres. Consequently, there is a possibility of mistaking the results of a cause in one sphere of action for those in another. Thus, the weight of $CHCl_3$-vapour in the air-way, under certain conditions of the respiratory machine, causes arrest of its movements. This physical action of $CHCl_3$ may be mistaken for its physiological action, which is assumed to be directly on the respiratory centre. The necessity for analysing the different spheres of $CHCl_3$-action, and its various modes of operating, each of which is confined to one sphere, and that only, becomes obvious.

$CHCl_3$ has three spheres of action. It is one of the two constituents of the mixed $CHCl_3$-air atmosphere which is breathed. Its vapour displaces a corresponding proportion of air, and in consequence thereof tends to induce defective aeration. This is the negative action of $CHCl_3$. It may be reduced to its lowest limit, as in the induction and maintenance of normal anæsthesia. But in the higher degrees of $CHCl_3$-action, the tendency is manifested in the discoloration of the blood. This interference with the normal constitution of the blood effected by the negative

action of $CHCl_3$ becomes a source of difficulty in the investigation of its physiological action. For it is conceivable that $CHCl_3$ may act upon the blood, and that its physiological action may be confined to that tissue. And it is probable that its negative action diverted the course of inquiry from this quarter of the field of investigation. By virtue of its density, $CHCl_3$-vapour tends to oppose an obstacle to the action of the respiratory machine. In ordinary circumstances, when $CHCl_3$ is the only agent in operation the tendency is not obvious. But the conditions which are affected by $CHCl_3$-action and which react upon it do not always remain the same. Variations may occur in any one of the components of the respiratory machine. And it is in these abnormal conditions that the tendency becomes manifested. This is the physical action of $CHCl_3$.

$CHCl_3$-vapour is absorbed into the blood, is assumed to circulate in it and to be carried to all the tissues of the body. The study of its physiological action was restricted to the spinal centres—the respiratory centre and the heart. It was attended by difficulties which were not properly recognised. In the first place, both its negative and physical actions were ignored. In the second, causes acting collaterally with it

were not isolated. It is certain that the lines of inquiry originally pursued are not wholly rational. And the question remains, How far are they partially so? or are they so at all?

$CHCl_3$-vapour may be introduced into the system with or without complication of the respiratory machine, according to the method of administration adopted. And during the procedure arrest of respiratory movements may occur at any moment. For, before the onset of unconsciousness, volition may be exercised, and take the form either of inhibition or arrest of the action of the respiratory machine. Too large a proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere predisposes to these results of voluntary action at the beginning of the administration. It operates by inducing a feeling of suffocation, which is more opposed by those of a fearful, and less by those of a sanguine, temperament. The object of the graduated method is to prevent the action of this predisposing cause.

The causation of respiratory arrest during the period of the induction of unconsciousness may be related to volition, and it is therefore necessary to exclude this possible causal factor in the investigation of the action of $CHCl_3$ upon the respiratory centre. Volition may be the sole cause of the arrest of respiratory move-

ments, which is then simple—*i.e.*, the result of a single cause. It may act in combination with a respiratory overdose of $CHCl_3$ to produce a complex form of respiratory arrest.

The influence of volition is removed when unconsciousness is induced. And during the maintenance of the lowest degree of $CHCl_3$ unconsciousness—*i.e.*, normal anæsthesia—respiratory arrest, when it occurs, is invariably preceded by an abnormal state of the respiratory machine.

The abnormality is not always the same in kind, but presents two different characters—the one of obstruction, the other of inhibition. The dissimilar periods antecedent to respiratory arrest have an important bearing on the relationship of $CHCl_3$ to the respiratory centre. For in this sphere of its action, $CHCl_3$ can only have one mode of operating. Assuming that it directly affects the centre, the question remaining for decision is, Which of the following groups is identified with its action—1, increased activity of the respiratory machine; 2, reduced action of the respiratory machine? The former is the result of stimulation, the latter of inhibition of the respiratory centre. These are opposite conditions. Now it is known that $CHCl_3$-action is causally associated with increased frequency of respiration, which is the

result of stimulation of the respiratory centre. It follows, therefore, that it cannot be causally associated with the inhibition of that centre. And the inference is drawn that another agent is in operation, whose influence on the centre is superior to that of $CHCl_3$. A group of instances of respiratory arrest is thus isolated, in which $CHCl_3$ is shown to have an influence on the respiratory centre. Is this influence sufficient to cause exhaustion of the centre? The answer to this requires the following analysis.

The degree of $CHCl_3$-result on the centre of respiration is maintained in a state of constancy. The records of these instances show that, in the course of normal anæsthesia, the frequency of respiration, instead of remaining at the rate of 28, which is normal for the first period, is still further accelerated during subsequent ones. And the amount of acceleration tends to increase progressively. Inference from this fact leads to, 1, the presence of a causal factor acting collaterally with $CHCl_3$; and 2, variations of the degree of its action. The combined action of $CHCl_3$ and this causal factor may be associated with respiratory arrest. But the anæsthetic degree of $CHCl_3$-action, operating in these instances, is not associ-

ated with respiratory arrest in all the stages of its progress, but only in one—viz., the terminal. Assuming that this phenomenon is the result of exhaustion of the respiratory centre,—for it is not yet proved to be so,—it follows that the physiological action of $CHCl_3$ on the respiratory centre cannot be taken to be its sole cause before the influence of this collateral factor is excluded. In this particular group of instances the action of $CHCl_3$ is limited to the degree of anæsthesia. But it may appropriately be argued that because the anæsthetic degree of $CHCl_3$-action is not associated, when acting alone, with arrest of respiratory movements, it does not therefore exclude the possibility of its causing exhaustion of the respiratory centre when the degree of its action is increased. For the degree of its effect is directly proportioned to it, and is one of the determinants of the results. A sufficiently large quantity of $CHCl_3$ circulating in the blood may, therefore, on supposition, cause eventually exhaustion of the centre. But it is impossible to produce pure plus $CHCl_3$-results, by the way which is commonly adopted, of its introduction into the blood through the lungs. For the increase of the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere is associated with a corresponding

decrease of the proportion of air. Deficient aeration indirectly affects the respiratory centre, by increasing the proportion of CO_2 (or diminishing that of OXy). Thus $CHCl_3$ does not act alone on the centre. And it is (assumed to be) circulating in the blood, which is in a condition of deoxygenation. If, under these abnormal circumstances, arrest of respiratory movements takes place, and is explained by exhaustion of the respiratory centre, then it is clear that all of the exhaustion is not due to the direct action of $CHCl_3$. What can only be affirmed is that $CHCl_3$ is one of two factors affecting the respiratory centre, and acting simultaneously, antecedent to the occurrence of respiratory arrest. But, assumed to be of central origin, the next point to be determined is, how much of the complex result is caused by the direct action of $CHCl_3$?

A second argument against the stimulant-exhaustion hypothesis is found in the exceptional character of the respiratory centre. It offers a greater resistance to the forces of exhaustion than is exhibited by any other centre. Particular knowledge is required of the limits of its resisting-power, and of the phenomena which accompany a diminution of its vitality. For the mere arrest of the action of the res-

piratory machine is not valid evidence of the loss of functional activity of the centre. Two data are necessary for the act of respiration—1, the activity of the respiratory centre; and 2, the ability of the respiratory machine to respond to it. The machine may be temporarily disabled. It is conceivable that, during temporary respiratory arrest, the centre preserves its activity. Its actual condition cannot be inferred with certainty, unless the impediment preventing the action of the respiratory machine is removed. And the abnormal condition of the heart, which is indirectly implicated, requires the immediate reduction of the impediment, and its complete removal in the shortest possible time. When this is done, the respiratory machine is in a favourable state to respond to the stimulation of the respiratory centre. If spontaneous respiration is resumed the conclusion is irrefutable, that the cause of arrest is not due to severe disturbance of the centre,—for then the recovery of the function would be delayed. But is it due to any disturbance at all? The fact is that, as soon as the respiratory machine is restored to its normal state, spontaneous respiration reappears, and immediately reaches its normal degree of efficiency. There is no

interval during which manifestations of the gradual recovery of the function of the centre are evidenced in the progressive increase of activity of the respiratory machine. When the latter is equal to the normal performance of its function, the respiratory centre shows that it also is ready to carry out its part in the act of respiration, without presenting any trace of exhaustion. The inferences are therefore, that, 1, during the period of arrest the centre is prevented from giving manifestation of its power to actuate the respiratory machine; and, 2, the source of arrest is in the inability of the latter to respond to the natural stimulus which proceeds from the centre, and is the fountain-source of respiratory movements.

§ 24. *Plural causation.*—Not only is the same result—*e.g.*, respiratory arrest—produced by causes which are most unlike each other,—*e.g.*, functional arrest of the action of the respiratory centre, mechanical obstruction, respiratory overdose of $CHCl_3$, and muscular exhaustion,—but it is also caused by combinations of these forces in different degrees of intensity. Thus, there may be a moderate degree of mechanical obstruction, and a relatively large proportion of $CHCl_3$-vapour in the air-way. Or mechanical obstruction may be the chief factor, and the

proportion of $CHCl_3$ relatively abnormal, and of secondary importance causally. These two combinations of the same factors do not, however, cause arrest of the action of the respiratory machine in the same way. In the former, the arrest appears early in the course of their combined action, is of rapid onset, and accompanied by slowing of the respiration. It is due primarily to the physical action of $CHCl_3$. In the latter (excluding, of course, complete obstruction), it is a late phenomenon, being associated with quick respiration, and is due primarily neither to mechanical obstruction nor to the physical action of $CHCl_3$, but to an intermediate cause — viz., exhaustion of the muscles of respiration. The supply of blood to the muscles is impaired both in quality and quantity. But the degree of its impairment does not remain constant, but undergoes a gradual progressive increase. The appearance of this intermediate cause is of note, inasmuch as it determines the relationship of the initial cause to the result, which occurs during the progress of its operation. And much of the perplexity pervading our notions of $CHCl_3$-action is removed, 1, by the isolation of the direct results of the forces which are known to be operating; and, 2, by determining whether

any one of them becomes an indirect or intermediate cause, producing results of its own. In the case of the respiratory muscles, the impairment of their nutrition, necessitated by the abnormal condition of the blood, tends to affect their functional capacity. But the same cause, — viz., the abnormal condition of the blood,—through its action on the respiratory centre, is indirectly responsible for an increase of the work which is done by them. The tendencies to exhaustion thus proceed from two results—one direct and the other indirect—of an intermediate cause which is the direct result of the primary agent.

Another example of a "result" becoming a secondary cause is found in muscle-collapse, followed by backward displacement of the base of the tongue. Fall of blood-pressure is associated with an increase of the normal degree of muscle-relaxation, which is one of the components of the state of anæsthesia. If the fall is severe, as measured by the disappearance of the pulse, the muscles are temporarily cut off from their blood-supply, and their condition is one of collapse. The tongue, itself a muscular organ and supported by muscles, is, under this abnormal condition, wholly subjected to the law of gravity. Its base is therefore displaced

backwards (or, if related to the supine position, downwards). Consequently its abnormal position encroaches upon, and may in some circumstances completely obstruct, the upper aperture of the larynx. It thus causes a greater or less degree of obstruction to the passage of air from the outside to the alveoli. The result—viz., mechanical obstruction in the air-way—is indirectly, not directly, caused by the complication. It is of practical importance in that it is the means of ultimately bringing the alveolar circulation to a standstill after the oxygen below the seat of obstruction has been absorbed. And, while it continues operating, it obviously retards the restoration of the normal action of the heart. The direct result of the complication—viz., the disappearance of the pulse—is of secondary practical importance. And the attempt to treat its assumed cause—cardiac weakness—directly is fraught with danger; for danger exists in delaying the relief of the right ventricle. This relief consists in the conveyance of air "to the alveoli." And it is forthcoming on the removal of the source of obstruction.

These two examples illustrate the influence of intermediate causation. They explain some of the differences which are found in "results" such as, 1, the early or late appearance of res-

piratory arrest; and, 2, the mode of its onset. And thus they serve as aids in the solution of the $CHCl_3$-problem.

There are, however, means other than those provided by $CHCl_3$-action by which respiratory arrest may be effected. They exist in the interaction of two causes, which may be either concurrent or in opposition. The following is an example of the former. The state of anæsthesia has been maintained for a period of 15′. At the end of it the character of the respiratory movements is altered. The action of the respiratory machine is now inhibited, and despite the occurrence of complication, the amount of $CHCl_3$ in the $CHCl_3$-air atmosphere is unchanged. The relationship of this amount of $CHCl_3$ to the action of the respiratory machine is no longer the same. During the one period the amount of $CHCl_3$ is normal, and the action of the respiratory machine normal; during the other the amount is relatively abnormal, because the action is abnormal. The difference is one of degree only, but it is followed by its consequences. Two causes are co-operating: one is the reflex inhibition of the respiratory centre, the other the physical action of $CHCl_3$, which is uncounteracted. The proportion of $CHCl_3$ which is adjusted to the normal action

of the respiratory machine becomes a relative respiratory overdose when that action is inhibited, by reason that the power which is needed to expel the contents of the air-way is unequal to the task. The weight of the mixed atmosphere is consequently to some extent uncounteracted, and leads in course of time to arrest of the action of the respiratory machine. And it is easy to perceive that arrest, dependent upon this complicated causation, will be more quickly induced when the initial proportion of $CHCl_3$ is an absolute overdose than in the instance of a relative one. In the former contingency, the interval between the accession of inhibited respiration and the onset of arrest may be so short as to create confused notions of its origin; whereas, in the latter, there is ample opportunity to observe the results of an impediment to the progress of a complication, to isolate the source of disturbance, and to counteract its effect. The disturbing factor being a relative respiratory overdose, the proportion of $CHCl_3$ is diminished in order to meet the requirements of the abnormal action of the respiratory machine.

But instead of acting concurrently, two causes may oppose each other. The essential datum, antecedent to the natural act of vomiting, is the arrest of the action of the respiratory ma-

chine at the end of full inspiration. It is effected by the stomachic arrest of the function of the respiratory centre. It is not a phenomenon of primary importance, but simply an incident appearing in the course of a natural function. In order to a full inspiration, two requisites are necessary—1, normal condition of the lungs; and 2, air-way free from obstruction, mechanical and physical. If, therefore, pulmonic congestion or a temporary excess of $CHCl_3$ in the air-way is present, full inspiration is prevented. Respiratory arrest, it is supposed, occurs during some stage of the progress of the latter. It will continue so long as the cause opposing the normal performance of a subsidiary function of the respiratory centre remains in action. The removal of the impediment is followed by the completion of full inspiration, and the expulsion of the contents of the stomach. And it is only through this procedure that the centre of respiration is released from the control which is reflexly exercised over it by the abnormal condition of the function of the stomach.

§ 25. *Verification.*—When a cause is put or goes out of action, its results disappear. One of the difficulties affecting the solution of the $CHCl_3$-problem is this: the phenomena ap-

pearing in the course of its operation derive from reflex as well as mechanical causes, and, in the case of the former, an appreciable interval exists between the cessation of the active agent and the return to the normal. The interval is necessitated by sympathetic changes effected by the reflex source of complication. Thus, in functional arrest of the action of the respiratory centre, there is practically a simultaneous fall of blood-pressure; and while it lasts the complexion undergoes a progressive increase of discoloration, due mainly to venous distension. When respiration is spontaneously resumed, the complexion does not at once become normal, nor does the pulse immediately reach its normal degree of tension; but they do so after an interval. Now, the cause of discoloration is temporary interruption to the normal supply of air to the alveoli, and of the fall of blood-pressure, the sympathetic stimulation of the vaso-motor centre. The resumption of respiration is immediately followed by a free supply of air to the alveoli—the air-way being supposed to be normally patent. The result of this is twofold,—the degree of oxygenation of the blood is increased and the degree of pulmonic congestion diminished. The alveolar circulation—reduced to a minimum

during the period of arrest—is thus improved, and the improvement continues until the normal relationship between the circulatory and respiratory systems is restored. The consequence, therefore, of the resumption of the respiratory function is not associated with the immediate restoration of normal conditions; and seeing that it is restricted to the supply of air to the alveoli, an interval of time must elapse before their appearance. The rate of rapidity with which the normal is reached varies according to the degree of pulmonic congestion, induced by the varying degree of disturbance to which the respiratory machine has been subjected by a relative respiratory overdose.

Reflex causes are without our control when they happen in the course of $CHCl_3$-action. It is impossible to counteract them. They run their natural course. But their progress may be opposed by some disturbing factor, which may be dependent on $CHCl_3$ or independent of it. A reason is thus adduced in favour of keeping the action of $CHCl_3$ under control.

The presence of a reflex cause in operation is indicated by its results. For example, in the course of normal anæsthesia disappearance of the pulse occurs suddenly, followed by rapid decline of respiratory movements. The air-way

is maintained normally patent, for the treatment consists simply of an efficient supply of air to the alveoli. The result of the original cause of complication is to divert the blood from the main circulation into the portal system. In its natural return to the main circulation the blood has to pass through the lungs. Hence the need of air in the alveoli. But before the pulse returns the left ventricle must be sufficiently supplied. Before the left ventricle is sufficiently supplied, the respiratory function must be restored to the corresponding degree of efficiency. The respiratory machine is, therefore, the first to give external manifestations of recovery; and these appear in slight movements of the abdomen. For the centre of respiration, which is secondarily, not primarily, affected, does not immediately proceed to normal activity after the severe disturbance it has experienced, but regains its power gradually, and yet comparatively quickly, when the comparison is made with the gradual recovery from the result of depressant action. There is a progressive increase of the range of abdominal movements until the lower thorax comes into action, when the pulse is perceptible. And as the respiratory movement extends to the whole chest, so the strength of

the pulse increases until it becomes normal, after the restoration of the normal action of the respiratory machine.

The removal of an active mechanical cause is followed by an immediate change of results. Duskiness is present with abnormal frequency of respiration. The action of the respiratory machine is abnormally increased. But the pupil remains normally contracted. The cause of the complication is backward displacement of the base of the tongue, leading to some degree of mechanical obstruction in the air-way. On replacing the base of the tongue in its normal position, two changes are immediately apparent: the action of the respiratory machine becomes less vigorous and duskiness less intense. The degrees of these conditions become reduced. They do not, however, reach the normal at once. There is an interval, longer or shorter, between the removal of the agent and the complete disappearance of the results with which it is associated. These results are direct and indirect. In the case of mechanical obstruction, one of the direct results—viz., pulmonic congestion—becomes an intermediate cause. The degree of pulmonic congestion is determined by, 1, the degree of obstruction, and, 2, the length of time during

which it operates. And the interval required for the removal of all the abnormal results is determined by the degree of pulmonic congestion.

Arrest of respiratory movements may be induced by mechanical obstruction, acting either as the sole cause in its simple, or as the principal factor in its complex, causation. In either contingency, the removal of the obstruction is followed by the immediate reappearance of some degree of respiratory movements. (It is assumed that there is no delay in removing the complicatory cause, but that it is rendered inactive immediately after the occurrence of arrest. For if there is delay, the conditions of the circulatory and respiratory systems, instead of remaining the same, undergo additional changes, either of degree, as in the increase of pulmonic congestion, or of kind, as in the occurrence of distension of the right ventricle. And neglect of these subsequent changes introduces a fundamental error into the investigation of the causation of the initial abnormal phenomena, of which they are the terminal stages.)

But respiratory movements, on their reappearance, do not exhibit the same degree of power. In the instance of simple mechanical obstruction, the return to the normal is of very short

duration. But in the instance of inhibited respiration, converted by obstruction into arrest, the removal of the mechanical cause is not very early followed by normal respiration, for the reason that the cause of inhibition is still in operation. Here respiratory movements reach that degree of reduced action which corresponds to the degree of inhibition of the respiratory centre present at the time of arrest. And they continue in the condition of inhibition until the centre is released from disturbance, after which they return to the normal.

Respiratory arrest may take place, and yet no movements reappear immediately after the replacement of the base of the tongue in its normal position. But they resume their work at the end of a short interval, the duration of which extends over a few seconds only. What is the significance of this interval? It signifies the presence of a source of obstruction to the passage of air. What is this source of obstruction? It is a temporary excess of $CHCl_3$-vapour in the air-way. Now this respiratory overdose of $CHCl_3$ is removed by the process of diffusion. And in order that the physical obstruction thus caused by an excess of $CHCl_3$-vapour shall be diffused as rapidly as possible, the air-way is to be maintained normally patent.

A few seconds are needed for its accomplishment, and the additional cause of respiratory arrest being thus removed—viz., the inability of the respiratory machine to expel the abnormally heavy contents of the air-way—respiration is resumed.

Again, arrest of the action of the respiratory machine may take place, and may not be followed by spontaneous resumption of its function after the removal of both mechanical and physical causes of obstruction. And in order to ensure the removal of the latter, the abnormal contents of the air-way are to be artificially expelled immediately after the occurrence of arrest. What is the explanation of the non-recovery of respiratory movements? What is the cause preventing the respiratory centre from manifesting its functional activity? The answer to this question is supplied by the backward course of the phenomena under treatment. This consists in artificial respiration, which is at once applied after the expulsion of the contents of the air-way fails to be followed by respiratory movements.

The following are the conditions affecting the respiratory and circulatory systems when artificial respiration is begun: there is a surplus of blood in the venous system, and a deficiency

in the main arterial circulation; the chest walls oppose some degree of resistance to compression. In the course of artificial respiration this resistance gradually diminishes until it disappears. As it diminishes, so does the venous distension diminish, and as venous distension diminishes, so does arterial tension increase and become perceptible in the pulse. As the result of the disappearance of thoracic resistance, the veins are reduced to their normal condition, and this is followed by the return of the normal strength of the pulse. The normal balance between veins and arteries is restored through the intermediation of a variation in the condition of the lungs. There may be some disagreement respecting the causation of the disappearance of the pulse when $CHCl_3$ is in action at the time of its occurrence. In the present example, if $CHCl_3$ be assumed to be the cause of it, on the evidence that the pulse ceases before respiration, though the interval is of short duration, so short, indeed, as to cause different observers to doubt whether primary failure involved the pulse or respiration —venous distension still remains to be explained. $CHCl_3$ causes indirectly disappearance of the pulse. It does so on assumption by inducing syncope. But ordinary cases of cardiac syn-

cope are not accompanied by venous distension. The question then presents, How does $CHCl_3$ cause venous distension?

There can, however, be no disagreement as to the cause of the resistance of the chest to compression. For only two causes are known —1, mechanical obstruction in the air-way; and 2, pulmonic congestion. Now the former has been excluded. The cause, therefore, of the non-recovery of respiratory movements is pulmonic congestion. And it explains not only the disappearance of the pulse, but also the distension of the veins.

These do not, however, include all the causes of respiratory arrest. The examples above described are given in order to determine the presence of causes affecting one or another of the components of the respiratory machine, and able to produce its arrest, and to verify the conclusion by demonstrating that when these causes are put out of operation, their result — viz., arrest of respiratory movements—disappears.

§ 26. *The natural line of investigation.*—$CHCl_3$ is conveyed by the action of the respiratory machine to the neighbourhood of the alveoli, which it reaches by the process of diffusion. It is taken into the blood. But, before assuming that it is carried by the circulation to the

parts upon which it operates after the manner of an alkaloid, it is necessary to determine its relationship, 1, to the respiratory machine, and 2, the blood. For it is conceivable that under certain circumstances the weight of $CHCl_3$-vapour may be a causal factor of respiratory arrest, and therefore, before concluding that any given instance of arrest is the result of the depressant action of $CHCl_3$ on the respiratory centre, it is essential to exclude the physical action of $CHCl_3$, in order to remove a possible source of error.

It is also conceivable that a closer connection exists between the blood and $CHCl_3$ than that of simple solution. And it becomes necessary, therefore, either to disprove that there is any such intimate connection, or to determine what the actual relationship is, if there be one.

The respiratory machine and the blood are the "parts" which are first affected by the action of $CHCl_3$. And in order to ascertain the influence which they exercise over it, the results are divided into two groups: 1, those occurring when their conditions are normal; and 2, those occurring when their conditions are abnormal. But a difficulty is presented by the different degrees of $CHCl_3$-action. For the amount of $CHCl_3$ determines the degree

of action, and different degrees are associated with different sets of phenomena. Thus there is one set of phenomena composing the state of anæsthesia, and another the state of narcosis. It thus becomes necessary to standardise $CHCl_3$-action in order to remove a source of error. For unless this is done it will be impossible to ascribe differences appearing in results to their proper origin—viz., some abnormal condition either of the blood or respiratory machine.

But the maintenance of the constant state of anæsthesia provides just the very advantage needed for the elucidation of the perplexing $CHCl_3$-problem. It makes possible an accurate observation of "new states" intervening in the course of $CHCl_3$-action, and therefore of the study of their causes. For it is obvious that, if two agents are operating simultaneously, it will be impossible to determine what part of the intermixture of results is due to either, unless the action of one of them is kept constant and its results known. (In the case of $CHCl_3$-action, an additional difficulty is introduced by the fact that the results of a given degree of it are constant only for a period. But this difficulty is overcome, and constant results maintained by a progressive diminution of the amount administered.) Let us suppose

that a "state" is complex,—and we may extend the supposition to a phenomenon, for phenomena are simple or complex, according as they derive from a single cause or a combination of causes,—and that its origin is the object of inquiry. The rational procedure is first to analyse it into its simple components. But the component states may have one or more phenomena in common—*e.g.*, abnormal action of the respiratory machine. It remains, then, to determine the part which each of the agents plays in the causation of this complex abnormality. But instead of arriving at the causation by inductive reasoning, a bias is entertained in favour of $CHCl_3$, and although another cause may be admitted to be present and in action, it is assumed to be unequal to explain the result. This tendency to fallacious reasoning is illustrated by the following example. In the course of normal anæsthesia, duskiness appears and increases. The power of the respiratory machine is gradually increased. But the pupil remains contracted for an interval, after which it gradually dilates. Subsequently, the breathing becomes "shallow," and is confined to the abdomen. Arrest of respiratory movements will occur if not counteracted.

Now when duskiness appears, the amount of

$CHCl_3$ has already been reduced in accordance with the principle of diminishing resistance. Thus a comparatively large amount of $CHCl_3$ is associated with the natural colour of the complexion, and a comparatively small amount with duskiness. With regard to the respiratory machine, its power increases at first as the degree of $CHCl_3$-action diminishes. Afterwards, when the reduced amount of $CHCl_3$ is kept constant (during its corresponding interval), respiration proceeds towards arrest. A larger amount had previously, during the normal part of the case, been administered, and was accompanied by normal respiration, which continued constant; but in the later stages of the state of complication, a smaller amount is accompanied not by a constant degree of abnormal respiration, but by an increasing degree of it. Let us suppose that arrest of respiration actually takes place, and also that it is assumed that $CHCl_3$ is the cause of it. The attempt next follows to construct an hypothesis which shall explain how $CHCl_3$ produces respiratory arrest. Such an hypothesis must agree not only with one condition of the respiratory machine, but also with all the variations of its action antecedent to and following upon that condition; for after the occurrence of respiratory

arrests, irregular movements of the chest may supervene. The hypothesis of the depressant action of $CHCl_3$ on the respiratory centre explains the causation of respiratory failure, but it does not explain why, 1, paralysis of the centre follows so quickly upon a comparatively short period of increased activity; and, 2, the depressant result on the centre increases as the degree of $CHCl_3$-action diminishes. Thus the fallacy of the wrong cause involves incompatibility between matters of fact, which are the subjects for causal treatment, and the hypothetical cause which is brought forward to explain them.

The fact that an hypothesis does not account for all the phenomena which are dependent on it argues the presence of some other agency. This does not necessarily exclude $CHCl_3$, either as a direct or indirect cause of respiratory arrest. For $CHCl_3$ has a physical as well as physiological action. What it excludes is the assumed mode of $CHCl_3$-action on the respiratory centre. Thus, $CHCl_3$ may possibly cause arrest of the action of the respiratory machine in some direct way other than that of paralysing the respiratory centre; or, it may act indirectly—*i.e.*, it produces a result which becomes the intermediate cause of respiratory arrest; or

there may be some independent agent acting simultaneously with $CHCl_3$; or there may be two or more causal factors entering into the causation of arrest of respiration. It is necessary, therefore, to discover the cause or causes which explain all the phenomena—viz., 1, the increased power of the respiratory machine; 2, the shallow breathing; and, 3, arrest of respiration.

Now, the initial set of abnormal phenomena point to defective aeration. This may be induced in two ways — either by reducing the normal proportion of air in the $CHCl_3$-air atmosphere, or by obstruction in the air-way. An absolute diminution of air is at once excluded, for, during a previous stage of the administration, a larger amount of $CHCl_3$ had been used, and therefore a smaller volume of air, without any manifestation of abnormal aeration. But during the early stages of duskiness the amount of $CHCl_3$ and the volume of air are kept constant for an interval, after which the latter is increased on the normal reduction of the amount of $CHCl_3$. If a causal relationship exists between the volume of air in the mixed $CHCl_3$-air atmosphere and duskiness, the degree of the latter will remain constant when the former is constant, and will

undergo a diminution when it is increased. But the fact is that during these two periods, characterised respectively by, 1, constant volume of air, and 2, increase of the proportion of air, duskiness progressively increases. It follows, therefore, that there is some other cause in operation which produces duskiness. And the only possible cause is mechanical obstruction in the air-way.

The increased activity of the respiratory machine is an indirect result of mechanical obstruction, the direct consequent of which is increase of CO_2 (or diminution of oxygen) in the arterial blood. This abnormal condition of the blood is causally associated with stimulation of the respiratory centre. Thus, the first of the three stages of the abnormal action of the respiratory machine is explained. What, then, prevents the continuous manifestation of increased respiratory activity, for its cause continues to operate? An alteration in the circumstances affecting the action of the respiratory machine.

If the conditions of the contents of the air-way, the lungs and the motor-power—the several components of the respiratory machine—remained constant, then increased activity would continue unopposed. But instead of the contents of the

air-way remaining constant, this change occurs —viz., an increase in the proportion of $CHCl_3$, resulting from the inability of the expiratory force to expel the normal volume of contents under the abnormal circumstance of mechanical obstruction. Thus the weight of the contents of the air-way increases, and opposes an increasing resistance to the action of the muscles of expiration. Hence the diminution of respiratory frequency, and the increased effort of the expiratory muscles to overcome the obstacle. This increased effort is not manifested; and because its result upon the expanding chest is of small extent, it is apt to be mistaken for weak or feeble action—a mistake which is very simply rectified by removing the cause which prevents the increased power of the expiratory muscles from being obvious to sight.

Two causes during the second stage of abnormal respiration are simultaneously in action. First, there is $+CO_2$ (or $-OXy$) in the arterial blood, tending to produce increased respiratory activity. Secondly, there is respiratory impediment of complex nature, consisting of mechanical obstruction in the air-way, due to the backward displacement of the base of the tongue, and physical obstruction, due to the density of $CHCl_3$-vapour. And the difference between the

first and second stages is thus isolated in an addition to the initial respiratory obstacle. For now, in place of simple mechanical obstruction, there is a combination of two causal factors of obstruction—1, mechanical; and 2, physical—*i.e.*, a respiratory overdose of $CHCl_3$. In the transition from simple to complex respiratory impediment, increased frequency of the respiratory machine predominates, until a given degree of respiratory obstruction is reached. The character of respiratory movements is then determined by the local conditions affecting the action of the respiratory machine.

The proximate cause of the opposite kind of breathing is a relative respiratory overdose of $CHCl_3$. It is dependent on mechanical obstruction, which is the ultimate cause; and it eventually leads to arrest of respiratory movements, the causation of which is explained by the final inability of the expiratory muscles to overcome the increasing resistance to their action.

The three stages of abnormal respiration are thus explained, not by a hypothetical mode of $CHCl_3$-action, but by causes which may be isolated and put out of operation. For if, at any point of time during the continuance of increased activity, the base of the tongue is

displaced forwards, respiration will become normal (*i.e.*, normal degree of $CHCl_3$-acceleration), and duskiness disappear. And if, during the period of obstructed breathing, $CHCl_3$ is removed, and the respiratory overdose thereby allowed to become dissipated, the distinctive character of obstruction will disappear, and the degree of duskiness be reduced: one cause being put out of operation, the results of the other are no longer disturbed, and the respiratory machine returns to its former abnormal condition of increased activity accompanied by duskiness—*i.e.*, mechanical obstruction is the only complicatory cause in action. The removal of simple mechanical obstruction will next be followed by normal breathing and normal colour of the complexion, thus affording an illustration of the successive removal of two causes which had previously been in action simultaneously. But the pupil begins to dilate in the course of obstructed breathing, and continues dilating gradually but progressively. What is the cause of this phenomenon?

Neither mechanical obstruction nor a respiratory overdose of $CHCl_3$ is equal to explain gradual dilatation of the pupil. For besides the disturbance which they effect in the respiratory machine, their only other result is de-

oxygenation of the blood. And deoxygenation of the blood, under these circumstances, is associated with contraction of the pupil up to the moment when continuity of respiration becomes interrupted, and then it dilates rapidly. There remains the physiological action of $CHCl_3$. The higher degrees of $CHCl_3$-action are associated with corresponding degrees of dilatation of the pupil. In the example under consideration there is excess of $CHCl_3$ in the air-way: thus the condition favourable to its absorption in more than the normal quantity into the blood is present. Thus the three phenomena—duskiness, abnormal action of the respiratory machine, dilating pupil—are explained. And the explanation involves all the three actions of $CHCl_3$. First, the normal proportion becomes relatively abnormal on the supervention of mechanical obstruction. The negative action, therefore, comes into operation. Secondly, the physical action comes into play at the same time. Mechanical obstruction prevents the expulsion of the normal volume of the contents of the air-way. Consequently more than the normal amount of $CHCl_3$-vapour remains, and the proportion of the residual vapour is increased at the end of each succeeding inspiration. The tendency to a gradual rise of the proportion of

$CHCl_3$, relatively to that of oxygen, in the respiratory passages is thus unchecked. Eventually the weight of the retained $CHCl_3$ resists the efforts of the expiratory muscles, and leads to obstructed breathing, ending in arrest of respiration. Thirdly, there is the physiological action, a representative of which is the dilated pupil.

And here we may illustrate the danger of inferring a false mode of operation on the part of $CHCl_3$ in the production of respiratory arrest. $CHCl_3$ is the chief causal factor in the case above described. But it does not cause it by acting on the respiratory centre, but by its physical action in the air-way. And the proof that it does so resides in the fact that when its undue weight is put out of operation, respiration is spontaneously resumed. Thus, to complete the description of the above case: immediately after the onset of arrest of respiratory movements, the base of the tongue is replaced in its normal position. Inspiratory movement does not at once follow upon the removal of mechanical obstruction, for the reason that the excess of $CHCl_3$-vapour in the air-way is allowed to be diffused, instead of being forcibly expelled; and this requires an appreciable interval of time. Hence the explanation of the

pause between the treatment and the restoration of spontaneous respiration. It is a valid one, because, 1, there is no other agent but $CHCl_3$-vapour in the air-way on the continuance of arrest after the removal of mechanical obstruction; and 2, it is a physical truth that a heavy vapour, as compared with a less dense one, requires a longer time to become diffused into the atmosphere. And in the case of the lungs, the air-way of which is composed of innumerable small channels, communicating by means of an opening which, when normally patent, is not conducive to the most rapid rate of diffusion, a natural obstacle is opposed to the outward passage of $CHCl_3$-vapour.

But suppose that in another and like instance the heavy contents of the air-way are forcibly expelled. The cause of respiratory arrest, instead of being less, is more rapidly put out of operation. And the consequence is that spontaneous respiration is at once resumed. Thus the predisposing cause of respiratory arrest, under the given conditions, is mechanical obstruction, the determining cause a relative respiratory overdose of $CHCl_3$. The result of the former is the development of an abnormal condition which favours the tendency, previously in check, of $CHCl_3$ to act as a heavy vapour.

But these two agents, mechanical obstruction and the weight of $CHCl_3$-vapour, may present differences in the initial degrees of their action. And either of them may also vary during the progress of its operation. Thus the degree of mechanical obstruction, slight at the beginning, may gradually and almost imperceptibly increase, or if there be a local favouring condition —*e.g.*, muscle-emaciation or an abnormally large tongue—it will tend to increase with less or greater rapidity. The weight of $CHCl_2$-vapour may undergo an absolute variation, unless the initial amount is limited to the anæsthetic degree of action, when it undergoes a relative variation. And new phenomena appear when the combination of these variant agents is favourable to them, as is shown in the more or less rapid expansion of the chest in some instances. Thus there can be no absolute uniformity of results in the different examples of this group, though there is a fundamental resemblance between them. For absolute uniformity is only possible in these circumstances —1, sameness in the conditions of the parts affected; and 2, sameness in the degree of action of the cause, or in the case of a combination of causes, of each of its components.

In like manner, all other abnormal states are

subjected to the same rigorous analysis. The cause or combination of causes of each is isolated. The results of all the possible variations of the conditions which may affect their progress are reached by abstract treatment. And the ways in which dangerous states may be produced are clearly defined. It is then ascertained that one of these conditions is present in a concrete example. The course of the phenomena in the abstract are compared with their concrete development, and demonstrated to be in conformity with experience. With the necessary phenomena, then, it becomes possible to reconstitute the successive stages of examples terminating in crisis: to indicate when a new agent comes into operation, as—*e.g.*, from obstructed breathing—respiratory overdose is inferred; and also when an agent is undergoing an increase of degree of action, as in expansion of the chest, resulting from an increasing degree of intensity of the cause of obstruction.

§ 27. *The source of disturbance.*—$CHCl_3$-action may be the direct or indirect cause of the abnormal state. It may act directly as an absolute respiratory overdose, or indirectly cause either disappearance of the pulse or respiratory arrest. These results are avoided, however, by limiting the action to the degree of anæsthesia.

In the course of the anæsthetic action of $CHCl_3$, complications may occur, due to the operation of collateral agents. And they may be confined to the simple results of those agents. But, on the other hand, they may also be subsequently affected by some abnormal direct or indirect $CHCl_3$ results, or by the results of mechanical obstruction.

The possible sources of disturbance are thus comprised in three main groups. In the first, $CHCl_3$ is the sole cause; in the second, it accompanies without affecting the action of another agent; in the third, it accompanies and affects the action of another agent. To these are added two sub-groups, arising from the action of mechanical obstruction of dependent origin, which affects that of the complicatory agent,—

1*a*. $CHCl_3$-action not affecting the progress of the complicatory agent, but mechanical obstruction affecting it;

2*a*. Some kind of $CHCl_3$-action and mechanical obstruction both affecting the progress of the complicatory agent.

In the investigation of $CHCl_3$-action, it thus becomes essential to determine its relationship to the phenomenon or state the causation of which is under consideration. $CHCl_3$ may be

the sole cause of, or it may co-operate with, another agent to produce it. In either contingency the mode of operation of $CHCl_3$ is to be defined, and the nature of the phenomenon dependent upon it determined—*i.e.*, whether it is a direct or indirect product. For example, n the case described in the preceding section, obstructed breathing and arrest of respiratory movements are different degrees of the same direct result of a relative respiratory overdose the dilating pupil is the indirect result of the physiological action of $CHCl_3$; and duskiness—*i.e.*, deoxygenation of the blood—is the indirect complex result of two agencies, mechanical obstruction and the negative action of $CHCl_3$, both which lead to a diminution of the normal volume of air in the air-way.

§ 28. *Procedure in the study of the $CHCl_3$-problem.*—$CHCl_3$ may be the sole cause of the abnormality or crisis, and yet its mode of acting may be falsely deduced. On the other hand, $CHCl_3$ may have no part in the causation of critical phenomena, and yet they may be erroneously ascribed to its action. To obviate false conclusions, it is necessary to proceed step by step, and thus eliminate the introduction of errors on which they are founded. To this end investigation is first conducted with refer-

ence to the relationship of $CHCl_3$-action to the respiratory machine and the blood. Next, the attributes of $CHCl_3$, its instability, and the phenomena which are associated with different degrees of its action, are considered. And, lastly, the analysis of the causation of the different states of crisis is effected, and the part which $CHCl_3$ plays in them isolated and defined.

PART I.

THE PARTS ON WHICH $CHCl_3$ ACTS.

§ 29. *The respiratory machine and the blood.*— $CHCl_3$ is ordinarily conveyed into the air-way by the action of the respiratory machine. It is absorbed into the blood in the course of the function of aeration. The natural order of investigation is thus clearly portrayed. It is the determination of the relationship between, 1, $CHCl_3$-action and the respiratory machine; and, 2, $CHCl_3$-action and the blood.

§ 30. *$CHCl_3$-action and the respiratory machine.*— The inspiratory current reaches to the neighbourhood of the alveoli, into which the $CHCl_3$-air atmosphere is diffused. If any abnormal cause opposes the progress of the inspired air, as voluntary inhibition of the breathing or physiologic pulmonic congestion, the force of the current disappears before its normal object is attained. There is, therefore, a longer distance

between the alveoli and the source of their oxygen supply. And this entails a longer period for diffusion, which is the only means of communication between them. Conversely, when in instances of pulmonic obstruction the chest is compressed, not all the contents of the air-way are expelled, but only a portion of them, and it may be a very small portion. The air-way being maintained normally patent, the expelled contents are replaced by an equal amount of the normal atmosphere. But, before this reaches the alveoli, it has to be diffused through a longer channel than the normal, the length of which is determined by the degree of the initial abnormal condition of the lungs. In order, therefore, to assist the incoming air to reach the alveolar region, which is the end-object of artificial respiration, an interval of time is requisite before the succeeding compression of the chest is effected. The interval between successive compressions of the chest is thus seen to be of fundamental importance in the performance of artificial respiration. For if, instead of favouring the diffusion of air into the alveoli, communication between them and the external atmosphere is interrupted by the too early artificial expiratory current, it is not difficult to perceive that, in spite of the rapidity with

which artificial respiration is conducted, not enough air, or it may be no air at all, will reach the alveoli.

If the air-way be normally patent, but no respiratory movements taking place, aeration is continued by diffusion. If there is no excess of $CHCl_3$ in the normally patent air-way, the inefficiency of this mode is shown in the progressive diminution of frequency and increase of strength of the pulse, and in the progressive increase of duskiness. If, on the other hand, there is an excess of $CHCl_3$ in the normally patent air-way, the natural process of diffusion is more or less interfered with, and, consequently, the alveolar circulation, instead of a relatively gradual, is subjected to a rapid onset of a severe, degree of obstruction. The result of this abnormality on the action of the heart is reflected in the state of the pulse, which, after a few beats of increased strength, rapidly declines and disappears.

In arrest of the action of the respiratory machine the rate of the progress of the phenomena, directly and indirectly dependent on it, is determined by the degree of obstruction to the passage of air from the outside to the alveoli. Voluntary arrest may occur during the period of the induction of unconsciousness. A reason

is thus advanced against the use of too concentrated an atmosphere of $CHCl_3$; for in these circumstances control is lost over the physical properties which it possesses. In view of this contingency, it is necessary to watch the action of the respiratory machine in order that, as soon as any abnormality in it appears, immediate measures may be taken to clear the air-way of excess of $CHCl_3$-vapour, should it happen to be present.

§ 31. *The physical action of $CHCl_3$; respiratory overdose.*—The $CHCl_3$-air atmosphere is heavier than air. Its weight and mobility are determined by the amount of $CHCl_3$. Hence, the density of its vapour is an important factor in abnormal action of the respiratory machine, as also in its inaction. For when present in excess in the air-way it tends to gravitate: in the former, leading to arrest and introducing perplexity into its assumed physiological explanation; in the latter, opposing greater difficulty in the way of its forcible expulsion, and thus prolonging for an appreciable interval the distension of the right ventricle.

The weight of $CHCl_3$-vapour comes into play, when the conditions are favourable, in the act of respiration, for more power is needed to expel a heavy atmosphere. And

there is the resistance of the outside air to be overcome, which is, relatively to the new condition, greater than the normal. Within a certain limit of density the normal respiratory machine adapts its action to the requirements of the mixed $CHCl_3$-air atmosphere and preserves its efficiency, the index to which is the normal aeration of the blood. But if this limit is exceeded, the action of the machine becomes abnormal: the abnormality appearing in the incompletion of the object of normal expiration, which is the expulsion of the normal volume of respiratory contents, and arising from the inability of the muscles of expiration to fully discharge the extra duties which are imposed on them. Thus an abnormal proportion of $CHCl_3$-vapour remains in the air-way after expiration, and forms the starting-point of its accumulation there. If the initial overdose is large and rapidly administered, the accumulation ot $CHCl_3$ in the air-way proceeds rapidly, impedes the action of the respiratory machine, and may cause a temporary arrest of it, which is removed by the diffusion of the vapour within after that without has been lost by evaporation, supposing that nothing in the meanwhile intervenes to prevent it.

If the initial overdose is small, but the in-

terval between its successive applications too short, the accumulation takes place gradually. The residual $CHCl_3$-vapour, at first mobile, becomes less so as it increases in amount and tends to gravitate. It opposes the passage of the mixed atmosphere, of which the proportion of $CHCl_3$ is constantly being reduced by evaporation, to the alveoli. And as one of the results of this obstruction the complexion becomes unduly dusky—*i.e.*, the degree of duskiness corresponding to the displacement of air effected by the initial overdose is exceeded.

The presence of physical obstruction is further illustrated by the following example. There is arrest of respiratory movements; the lint containing $CHCl_3$ is at once removed, and the base of the tongue is maintained in its normal position, so as to ensure the normal patency of the air-way, for it is upon this condition that the rate of recovery depends. There is thus free communication between the outside air and the alveoli, so far as mechanical obstruction is concerned, but the air-way is occupied by the $CHCl_3$-air atmosphere, which had been administered before the onset of arrest. Now, the conveyance of air to the alveoli brings immediate relief to the impaired alveolar circulation, and this is reflected in the immediate

improvement of the pulse, which becomes increased in frequency and reduced in strength; the latter variation of the main circulation arising from the return to favourable surroundings replacing the former variation — reduced frequency and increased strength, which follows upon retardation of the alveolar circulation. But in a particular instance no such immediate perceptible improvement of the pulse takes place. On the contrary, the pulse may still further decline, or even disappear, according as the excess of $CHCl_3$-vapour in the air-way is less or greater. What happens is this: between the application of the means of recovery and the perceptible improvement or reappearance of the pulse, there is an appreciable interval. And it is during this interval that the physical obstruction opposed by $CHCl_3$-vapour is being removed by diffusion. As, however, it is not completely removed at first, its result on the alveolar circulation still continues, though in a less degree of intensity, consequently the pulse continues to decline. But the ultimate cause of its improvement is in operation, though its manifestation is delayed; for with the progressive disappearance of the excess of $CHCl_3$-vapour, respiratory movements spontaneously reappear, and as now there is no obstacle to the

free communication between the outside air and alveoli, the alveolar circulation rapidly returns to the normal, and, consequently, also the main circulation.

In this example there is assumed to be no other complication but an excess of $CHCl_3$-vapour in the air-way. But it is not always found acting alone. It may be associated with voluntary inhibition or arrest of the action of the respiratory machine during the period of the induction of unconsciousness, as also with mechanical obstruction in the air-way from backward displacement of the base of the tongue during the course of unconsciousness. This displacement may be complete. When it is so, the course of the phenomena, dependent upon $CHCl_3$-vapour operating as an obstructant, loses its distinctive character. For instead of being gradually, respiratory arrest becomes, under this accidental condition, suddenly, induced. This suddenness resembles the mode of operation characterising reflex-action, which immediately attains its maximum result.

The accumulation of $CHCl_3$-vapour in the air-way may be called a respiratory overdose, in contradistinction to blood-overdose, which is the result of excessive action of $CHCl_3$ on the blood. For it is not a necessary inference that

because there is an excess of $CHCl_3$ in the air-way, therefore there is an excess in the blood. Absorption into the blood is determined by the rate of the alveolar circulation. A respiratory overdose tends to retard the alveolar circulation, and thus it exercises a control over the absorption of $CHCl_3$.

Respiratory overdose is the outcome of the physical action of $CHCl_3$, and the consideration of the variations of the $CHCl_3$ constituent of the $CHCl_3$-air atmosphere, and the variations of the action of the respiratory machine forms the physical side of the $CHCl_3$-problem as opposed to its physiological side. And not only its weight, but also its negative action, viz., the displacement of a proportionate amount of air, have to be separately considered in order to ascribe to each its due and proper results. For example, a given overdose of $CHCl_3$ is associated with increased activity of the respiratory machine, which is the result of stimulation of the respiratory centre, consequent upon the deoxygenation of the blood, which, again, is the result of defective aeration, the consequence of the displacement of air by $CHCl_3$. If the conditions of the air-way regarding its patency and the proportion of its contents remain the same, the increased activity of the respiratory machine

will remain at the same level for a period antecedent to the appearance of signs of exhaustion of the muscles of respiration. This is due to the negative action of $CHCl_3$. But one of these conditions does not remain the same; for after an interval of increased activity, and before the manifestation of exhaustion, the character of the breathing undergoes a change. It becomes obstructed from the coming into action of a respiratory overdose; it is an absolute respiratory overdose, by reason of the initial dose being an overdose. A relative respiratory overdose occurs when a variation of the action of the respiratory machine, independently of $CHCl_3$-action, intervenes in the course of normal anæsthesia, thus altering the normal relationship between it and the $CHCl_3$-air atmosphere. The breathing becomes obstructed, because under the new condition its power is unable to expel the normal volume of an absolutely heavy atmosphere.

In normal anæsthesia there is a minimum disturbance to the action of the respiratory machine, which is effected by controlling the $CHCl_3$-constituent of the $CHCl_3$-air atmosphere.

§ 32. *The components of the respiratory machine.* —These are—1, the air-way; 2, the lungs; and 3, the motor-power. Abnormality in any one of

them may lead to arrest of respiratory movements. It is necessary, therefore, to consider each in detail.

§ 33. *The air-way.*—Muscular relaxation is one of the concomitants of $CHCl_3$-action, and, in the case of the base of the tongue, leads to its displacement through gravitation. The epiglottis encroaches upon the upper aperture of the larynx, and so produces a degree of mechanical obstruction which gives rise to noisy breathing. Noisy breathing is thus an accidental, and not a characteristic, feature of the state of $CHCl_3$ unconsciousness. It is more pronounced in $CHCl_3$-narcosis than in anæsthesia, by reason of the greater degree of muscle-relaxation in the former, given initial normal muscles. But if the initial condition of the muscles is abnormal, as in emaciation or anæmia, the degree of noisy breathing is exaggerated, in anæsthesia, by reason of the greater degree of obstruction. In all instances, noise ceases when its cause is removed, by replacing the base of the tongue in its normal position.

Nasal stenosis is an abnormality varying in degree. In its more severe forms it is associated with mouth-breathing. To meet its requirements the normal method is adapted, so

as to avoid a feeling of suffocation and the appearance of duskiness. The lips are separated, and the rate of increase in the proportion of $CHCl_3$ regulated according to the degree of obstruction. This abnormality, when overlooked, is an origin of irregularity in the induction of anæsthesia. For the normal method, which is constructed for normal conditions, becomes, under the abnormal condition of the air-way, a form of rapid method, and is therefore associated with the result of that method, viz., a respiratory overdose.

In the case of laryngeal obstruction, difficulty with the air-way is again encountered. The end-object to be achieved is the transit of $CHCl_3$-vapour to the alveoli, without adding an artificial to the natural impediment to the action of the respiratory machine. It therefore demands delicacy in regulating the rate of increase in the proportion of $CHCl_3$. In some forms, and especially in diphtheria, the initial degree of respiratory obstruction undergoes a considerable degree of improvement towards the approach of unconsciousness. This is explained by the disappearance of "spasm" of some of the laryngeal muscles.

The relatively large tongue of infants, with the assistance of the act of suction, enables

them to prolong inordinately the voluntary arrest of their breathing when confronted with an initial overdose of $CHCl_3$. The base of the tongue is displaced backwards and surrounded by the pharyngeal walls. The nasal passages are thus shut off temporarily from the lower air-way. In order to restore communication with the larynx, it is necessary to displace the base of the tongue forwards, a procedure which is difficult of attainment, seeing that the pharyngeal muscles are contracted round it. This characteristic of "holding the breath" displayed by infants is the prime source of error affecting the amount which they need for the purpose of being rendered unconscious; for by far the larger part of the amount which is administered to them is wasted by evaporation. When the air-way is not unduly obstructed, and the application of the normal amount of $CHCl_3$ is timed so as to coincide with inspiration, it will be found that a very small quantity is required. The object is not to add to a difficulty which already exists. In all instances assistance is afforded at the beginning of administration by placing the finger between the gums. But in some, owing to its abnormal size, it is necessary to maintain the normal position of the base of the tongue throughout the administration.

The tongue may be rendered abnormally heavy by malignant disease, or by abscess or a cyst. There is, therefore, a tendency in such conditions to complete mechanical obstruction on the appearance of muscular relaxation. In order to obviate a possible result of this complication—viz., rigidity of the muscles of the jaw, consequent on rapid deoxygenation of the blood—it is necessary to introduce a gag before the onset of unconsciousness. The cause of obstruction, when it becomes operative, can thus be easily removed.

The same procedure is also necessary in enlarged tonsils and adenoids. For when the muscles relax the tonsils may meet, and so cause a considerable degree of obstruction when breathing is partially oral, and complete obstruction when it is principally so.

The use of the gag during the administration of $CHCl_3$ is to be conducted on rational principles. A too-widely opened mouth is necessarily associated with some degree of respiratory obstruction. And if the temporo-maxillary articulation is loose—*i.e.*, the articular surface of the lower jaw is easily displaced backwards—it will be associated with complete obstruction. The difficulty is overcome by partially closing the gag from time to time, and thus permitting

a greater degree of aeration of the blood. In these abnormal cases the amount of $CHCl_3$ is to be regulated by the degree of discoloration of the blood.

In the course of surgical operations upon the lower jaw, partial dislocation may be induced. It may be counteracted, and respiratory obstruction consequently avoided by supporting the angle. But should it happen that the application of this means is defective, or at times impracticable, it will be necessary, in order to prevent an undue degree of deoxygenation, to allow the blood to become normally aerated from time to time, by maintaining the base of the tongue in its normal position. Undue extension of the neck is followed after an interval by obstructed breathing. And as this result is gradually induced, it may lead to erroneous inference unless the $CHCl_3$-air atmosphere is correspondingly adjusted to it. Pressure on the trachea, and raising it from its natural position, as by the tracheotomy hook, are both followed by disturbance in the action of the respiratory machine, which in some cases may be manifested by its arrest. In such a contingency it is essential that the air-way should be free from an excess of $CHCl_3$-vapour.

Abnormalities of the air-way thus occupy a

position of first-rate importance in relation to the $CHCl_3$-air atmosphere. They explain the occurrence of some irregularities, both during the induction and maintenance of anæsthesia. Their influence, therefore, has to be taken into consideration and counteracted by the adjustment of the $CHCl_3$-constituent of the $CHCl_3$-air atmosphere to their several requirements, in order to avoid ascribing to the action of $CHCl_3$ results which are only partially caused by it.

§ 34. *The Lungs.*—Abnormal conditions of the lungs, *e.g.*, bronchitis, emphysema, phthisis, are associated with defective aeration. A diminution of the normal volume of oxygen in the atmosphere breathed is followed by manifestations of additional disturbance in the function of aeration. The introduction of $CHCl_3$ is therefore conducted on the principle that initial abnormal lungs require a longer period, as compared with that required by normal ones, for the purpose of adjusting themselves to the abnormal condition under which they are to carry on their function. The period varies according to the degree of the pulmonic abnormality. When, however, the degree of abnormality is moderate, it is apt to be overlooked. The normal method becomes, under these circumstances, a relatively rapid method, and

associated with the phenomena which are characteristic of it—viz., duskiness, obstructed breathing, and muscle-rigidity. The first indication of the presence of some abnormal condition is in the early appearance of an undue degree of duskiness. If, on its occurrence, the $CHCl_3$-air atmosphere is replaced by air, the degree of duskiness does not immediately diminish, as it would do, if the fault existed not in the lungs, but in the management of $CHCl_3$. On the contrary, it increases, and after reaching its limit begins to diminish, the rate of its progress being gradual. The explanation is that the initial abnormal lungs are subjected to a less or greater degree of physiologic pulmonic congestion: they do not unload themselves so readily as usual lungs do, and the delay in the supply of air to the alveoli, consequent upon the diffusion of the respiratory overdose, is followed by greater disturbance in the alveolar circulation, when it is initially of diminished volume, than in its normal condition.

In some instances the discharge of matter has to be anticipated. In the course of an operation on a consumptive subject, an attack of coughing supervened. About ten minutes after, and half an hour from the beginning of

the administration, during which the amount of $CHCl_3$ was limited to the degree of anæsthesia, an immediate arrest of respiratory movements occurred. The head and shoulders were at once lowered below the edge of the table, and the base of the tongue and the lower jaw displaced forwards. In this position duskiness rapidly increased, and the pupil became widely dilated; but after a short interval an ill-smelling matter escaped from the nose and mouth. During the period of the escape—and the quantity measured reached to half a pint—the duskiness of the complexion was replaced by lividity, and the pulse rapidly disappeared at the wrist. The base of the tongue was maintained in its normal position during the whole of this interval,—for upon the patency of the glottis depends the communication between the outside air and the alveoli, and it is essential that it should be, in such an emergency, absolutely normal. The first manifestations of returning aeration were observed in the immediate contraction of the pupil, and perceptible though slight alteration in the coloration of the complexion. These were subsequently followed by abdominal movements, extending to the thorax, and the reappearance of the pulse.

$CHCl_3$ may be administered in pneumonia both before and after the crisis. It is in these and suchlike abnormal conditions that the rate of increase of the $CHCl_3$-constituent requires, in particular, to be accurately regulated by the factors which determine it.

The result of change of position, necessitated by the operation, has to be considered in regard to the lungs. Thus, when the supine is replaced by the lateral position, the expansion of the lower lung is considerably impeded. Practically it is to be taken to be temporarily out of action. The amount of $CHCl_3$ has, therefore, to be reduced by one-half in order to meet the requirements of the new condition of the respiratory machine. An alteration in the general position may also be accompanied with a change in the position of the base of the tongue. Measures are therefore to be taken to replace it in its normal position if it is thus incidentally made to encroach on the upper aperture of the larynx. For the administration of $CHCl_3$ is dangerous through an abnormally narrow glottis, under any circumstances, unless its amount is proportionately reduced; and it becomes particularly so in the lateral position when no reduction is made. The danger consists in the induction of a respiratory overdose

which, if not detected and treated, leads to respiratory arrest.

§ 35. *The Motor-power.*—The increased activity of the respiratory machine, which is associated with moderate degrees of $CHCl_3$-narcosis, was formerly regarded as evidence of "efficiency." The inference was drawn simply from the character of the respiratory movements. And although duskiness is present, no relation was made between the two phenomena. In reality, the degree of increased activity is abnormal. But it is erroneous to infer that because it is "safe" for a given period—*i.e.*, relatively safe—therefore it is absolutely safe for all periods. This is shown by the complication which arises when the duration of the operation becomes prolonged. For that is the circumstance—viz., duration of $CHCl_3$-narcosis—which determines, according to its greater or less degree, the comparatively early or late appearance of arrest of respiratory movements from muscular exhaustion. Increased activity is associated with increased work. But the initial energy of the respiratory muscles being limited, and their nutrition being progressively impaired, while the power they are called upon to exercise increases, both relatively and absolutely, the time will necessarily arrive when they become

incapable of performing their function, even in the most inefficient manner. Now, duskiness implies impairment of aeration, and impairment of aeration implies abnormal action of the respiratory machine. Consequently the increased activity of the respiratory machine is not sound evidence for the safety of its working order. On the contrary, its appearance is significant of resistance against the normal performance of its function, which it attempts to counteract, but never succeeds in overcoming completely.

The initial power of the respiratory machine may be less than the normal, as in emaciation and acute illness. Consequently it is incapable of expelling a normal $CHCl_3$-air atmosphere with the requisite degree of efficiency. In these circumstances there will be a tendency to the early appearance of a severe degree of respiratory obstruction. But it is counteracted by equating the weight of the mixed atmosphere—*i.e.*, the proportion of $CHCl_3$ to the force which moves it.

Respiratory movements may be of small range. But they are not, on this account, necessarily "weak." For the muscles of respiration may be prevented from manifesting the full extent of their power through the presence of an abnormal condition. For ex-

ample, in the course of the induction of unconsciousness, given an initial normal state of the respiratory machine and the use of the normal method, the chest gradually expands. As the degree of expansion increases, the movements of the chest undergo a reduction in range in an inverse proportion. In the early stages of induction, voluntary inhibition is the contributory factor—the inhibited movements becoming progressively reduced in range: in the later stages, as the threshold of unconsciousness is approached, it is mechanical obstruction in the air-way, due to displacement of the base of the tongue, in circumstances which are favourable to its occurrence; and the action of the respiratory machine, not being complicated by inhibition of the centre, pursues its natural, though abnormal, course. If, in the first example, the $CHCl_3$-air atmosphere is displaced by air, the reduced respiratory movements gradually reach not their normal range, but that to which they are reduced by inhibition. In the second, the replacement of the base of the tongue in its normal position is followed by the gradual return to the normal range, even during the continued administration of $CHCl_3$, the necessary condition being that its proportion is normal. Thus in both examples there is proof

that the respiratory muscles are acting with a greater degree of power than is represented by their result. Just as in the compression of a tense elastic bag with a small aperture for the escape of its contents, the result upon it is small as compared with the great force applied, but is correspondent to it under the conditions. But if the aperture were larger, the result would also be larger in proportion. Thus the size of the orifice determines whether the result shall be large or small, when the same degree of pressure is used.

Complete mechanical obstruction may occur either during inspiration or at the end of expiration. When it takes place during inspiration, there is either no subsequent movement of the chest, or it continues, but with reduced range, and rapidly ceases. When it occurs after expiration, the air-way is empty, and, no resistance being opposed to it, the action of the respiratory machine continues with apparently normal power for the first three or four movements and then rapidly declines.

In any instance in which the respiratory movements are abnormal, it is not to be inferred that because the mixed atmosphere enters the air-way, therefore it reaches the alveoli. For there may be physical obstruction to its

passage, which continues operative, but begins to diminish in intensity when the mixed atmosphere is displaced by air. Respiratory movements, limited to the abdomen, may continue and yet an insufficient supply of oxygen reach the alveoli, or perhaps none at all (aeration being, under the circumstances, reduced to a minimum, inasmuch as it is dependent on the residual oxygen in the alveoli). Thus, though movements are present, it may be necessary to remove immediately the abnormal contents of the air-way. Delay in the application of this measure until all movements have ceased will obviously be associated with additional embarrassment to the function of aeration.

§ 36. *The state of the respiratory machine.*—1, The air-way and the lungs may both be normal; or 2, the air-way may be normal and the lungs abnormal; or 3, both the air-way and lungs may be abnormal. In each of these combinations the motor-power may either be normal or abnormal. Again, in each of these double combinations the $CHCl_3$-air atmosphere may be normal or abnormal.

Some of these conditions are permanent—*e.g.*, nasal stenosis, emphysema; others intervene in the course of $CHCl_3$-action. The intervening conditions are either under control,

as in mechanical obstruction and respiratory overdose (the consequence of fault in the method), or not under control, as in voluntary or stomachic inhibition of the respiratory centre. In the former they are removable; in the latter they run their natural course, but entail a modification of the details of the normal method to their several requirements. The various combinations of these conditions, including the $CHCl_3$-factor as a variant, supply a sufficient explanation of the appearance of "irregularities." For in order to a constant and normal state, it is essential that the factors which are associated with its production shall be, all of them, constant and normal. If, therefore, in the course of the application of the normal method some abnormality occur, its origin is to be found, not in the irregular action of $CHCl_3$, but in the presence of an abnormal condition which is its determinant, and to which the normal method has not been adapted. Thus, suppose the abnormality to be arrest of the action of the respiratory machine. Its cause may be in the machine itself. It is, therefore, necessary to exclude, 1, mechanical obstruction in the air-way; 2, respiratory overdose; and 3, exhaustion of the respiratory muscles, before we proceed to associate

$CHCl_3$ with direct action on the respiratory centre.

§ 37. *Control of the respiratory machine through the centre of respiration.*—The known agencies affecting occasionally the respiratory centre, so far as the $CHCl_3$-problem is concerned (and excluding its assumed direct action), are four. Of these, two affect the centre primarily, viz., volition and stomachic disturbance, and two secondarily, viz., emotion and stimulation of the vaso-motor centre. Voluntary is differentiated from stomachic inhibition by means of pallor, which is invariably associated with the latter. Stomachic disturbance is, however, of very infrequent occurrence during the period of induction. Voluntary inhibition requires the adjustment to it of the details of the normal method, until such time as the centre is released from control. Besides inhibition, voluntary arrest may occur at any moment in the transitional stage between consciousness and unconsciousness. It may be the last act of consciousness, and overtaken by the state of unconsciousness. To meet this possible contingency normal conditions of the air-way and lungs are to be maintained. For, though the cause is suspended, its result on the centre continues, nevertheless, for an appreciable interval. If,

in these circumstances, the conditions of the air-way and lungs are abnormal, diffusion of the respiratory contents into the atmosphere will be retarded, and, by implication, a tendency to rapid increase in the degree of pulmonic congestion will be manifested. An increase of CO_2 in the blood stimulates the respiratory centre. But no activity of the centre is manifested during the interval in which the proportion of CO_2 is increasing. If voluntary arrest of respiration is complicated by contraction, followed by rigidity of the muscles of the lower jaw, it becomes more or less critical by reason of the greater or less difficulty encountered in overcoming their resistance,—a procedure which is necessitated by the presence of mechanical obstruction in the air-way, arising from the backward displacement of the base of the tongue. Emotional disturbance of the cardio-inhibitory centre varies in degree. When it is severe, the accelerated action of the respiratory machine becomes unfavourable to the administration of $CHCl_3$, and determines its postponement for a few minutes. There is, besides, the possibility that an extreme degree of emotion may concur with initial cardiac weakness; and the further possibility that a weak heart may succumb to the violence of

emotion. For example: an elderly man who was known to have a "feeble" heart appeared pallid, but walked up to and lay down on the operating-table. In the course of surveying the conditions of the parts affected by $CHCl_3$, before its administration, it was discovered that, 1, respiratory movements continued, but of small range; 2, the pulse had disappeared; and 3, the pupil was widely dilated. Soon respiratory movements ceased. Death had occurred from primary cardiac syncope. If, now, $CHCl_3$ had been administered in ever so small an amount, or if the syncope had been delayed for two or three minutes, then a reason would be forthcoming for the assumed irregular action of $CHCl_3$.

The respiratory centre is sympathetically affected by stimulation of the vaso-motor centre. This kind of disturbance of its function is confined to the period of unconsciousness. It varies in degree according to the degree of stimulation of the vaso-motor centre. When this is moderate, the activity of the respiratory centre is increased, as manifested by acceleration of respiratory movements. When it is severe, the function of the respiratory centre is rapidly depressed, as manifested by the rapid decline of the action of the respiratory machine. But

there is no actual arrest of the respiratory function. It is reduced to a minimum, and immediately afterwards begins gradually to recover its normal activity.

Reflex arrest of the action of the respiratory centre occurs in the progress of stomachic disturbance. It is subservient to the act of vomiting.

§ 38. *Abdominal tension and fever affecting the action of the respiratory machine.*—Abdominal tension may be solid or fluid or both. In the severer degrees of it, it is counteracted to some extent by the voluntary effort of the patient. There is a tendency, therefore, when this is removed, to respiratory arrest. In view of this possible result, precaution is to be taken against a respiratory overdose which would obviously be associated with danger, arising from the inability of the respiratory machine to recover readily from its temporary state of embarrassment.

In fever the frequency of respiration is accelerated. This is not a favourable condition in the administration of $CHCl_3$. For it implies some degree of inefficiency of the function of aeration. The current of the inspired air, instead of reaching its normal destination, viz., the neighbourhood of the alveoli, stops short of

it. Consequently, the rate of diffusion is retarded. In extreme instances the degree of disturbance is determined by the degree of duskiness of the complexion. The normal $CHCl_3$-air atmosphere is brought into normal relationship with the alveolar region by the normal action of the respiratory machine. It does not apparently interfere with the process of diffusion, for it is associated with the natural colour of the complexion—*i.e.*, efficient aeration. In the abnormal condition of increased frequency of respiration, the process of diffusion is abnormal—*i.e.*, it is delayed. And it is this delay which is favourable to the gradual increase in the physical action of $CHCl_3$, if its proportion is not reduced, at necessary stages, to prevent its occurrence. There is always, in extreme instances, some degree of it induced by the action of $CHCl_3$. It is, under the circumstances, a necessary result, but a result which it is essential to maintain at its lowest possible degree of intensity.

These two factors—abdominal tension and fever—are adduced in order to show the importance of taking an accurate survey of the kind and degree of the abnormality of the respiratory machine, and of anticipating consequences that are likely to occur under certain

conditions of the $CHCl_3$-air atmosphere. It is also necessary to know how much may safely be effected by $CHCl_3$ in some extreme degrees of the former abnormality. Thus, when the tension of the abdomen is very great, it is impossible to induce anæsthesia without encountering a difficulty which might prove insurmountable. It is prudent, in such circumstances, to limit the action of $CHCl_3$ to a degree of semi-unconsciousness during the first stage of the operation—viz., opening the cavity of the peritoneum. After the escape of fluid, the action of the respiratory machine is relieved of some degree of its embarrassment, and the improvement thus effected in it permits of the safe transition from semi-unconsciousness to anæsthesia.

In the case of a high degree of accelerated respiration it is impossible to produce a pure $CHCl_3$ result. What is induced is a state of mixed unconsciousness—*i.e.*, $CHCl_3$ and $+CO_2$ or $-OXy$. The degree of the abnormal condition determines the limit of the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere. If this be exceeded,—and herein lies the danger of initial large doses, which are not equated to the requirements of the respiratory machine, —the result of respiratory overdose will be

manifested by the early arrest of respiratory movements.

§ 39. *$CHCl_3$-action and the blood.*—The blood is the first tissue with which $CHCl_3$ is brought into physiological relationship. That $CHCl_3$ exists as such in it has not been proved. But the assumption is made that $CHCl_3$, or one of its products, is carried by the blood to the heart and the respiratory centre.

The $CHCl_3$-air atmosphere contains less than the normal proportion of oxygen, by reason of the displacement of air by $CHCl_3$-vapour. There is a tendency, therefore, to impairment of aeration accompanying its use. But given a normally patent air-way, the tendency is not manifested by appreciable discoloration of the blood when the proportion of $CHCl_3$ is normal in the $CHCl_3$-air atmosphere. Within a certain limit the proportion of oxygen may be diminished without disturbance to the function of aeration, the reduction in supply being associated with increased frequency of respiration. This is due to the ability of living tissues, with one exception, to adjust themselves for a period to slight variations of the conditions affecting them without manifesting change in the normal discharge of the functions which they subserve. The exception is the respiratory centre, the

functional activity of which is stimulated by an alteration in the normal relation of CO_2 and OXy in the blood. But if a variation of condition be made to exceed the given limit, the power of adjustment possessed by the tissue will be encroached upon, and as the consequence thereof abnormal results will appear.

A proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere displacing a larger volume of air than the normal, is associated with immediate disturbance to the function of aeration, and consequently with discoloration of the blood. And the variations of these two factors—viz., the initial overdose of $CHCl_3$ and discoloration of the blood—are in a direct ratio to each other. The explanation is near at hand in the negative action of $CHCl_3$. For the greater the volume of air displaced, the greater is the impairment of the function of aeration, and this is manifested by the greater degree of discoloration of the blood.

Impairment of the function of aeration is also followed by distension of the pulmonic artery —*i.e.*, physiologic pulmonic congestion. Now, pulmonic congestion determines the rate of the alveolar circulation. And upon the rate of the latter the rapidity with which $CHCl_3$ is absorbed depends. But an initial large propor-

tion of $CHCl_3$ tends to slow the circulation through the lungs. And thus it carries with itself a check to its rapid absorption.

An excessive proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere defeats the object which is aimed at—viz., the quick suspension of the mental functions through the physiological action of $CHCl_3$. Besides, in the endeavour to enable $CHCl_3$ to affect the cerebral centres (according to the hypothesis) with undue rapidity, a degree of risk is run which varies directly with the degree of the initial overdose. The risk lies in the induction of a respiratory overdose which may be the product of $CHCl_3$ alone, or the combined result of $CHCl_3$ and a collateral cause. In either case there is a tendency to respiratory arrest, the causation of which may be falsely inferred.

But when no respiratory overdose results from an initial overdose of $CHCl_3$, the state of unconsciousness is not induced by its physiological action alone, but is caused partly by it and partly by its negative action. This is demonstrated by the following abnormal example, in which, after the onset of automatic respiration, the skin-incision is followed by return to consciousness. Of the two factors, $CHCl_3$ and $+CO_2$ (or $-OXy$), the degree of action of the

former does not suffice of itself to suspend the functions of the mind; and the latter, when present in the larger proportion, as is presupposed, does not produce a stable form of unconsciousness. The result of stimulation disturbs the constitution of the complex cause of unconsciousness. For the $+CO_2$ factor is easily displaced by oxgyen through the increased inspiration consequent upon the application of a stimulus of the necessary degree of intensity, and leaves the proportion of $CHCl_3$ unequal to maintain the state of unconsciousness.

The $+CO_2$ factor is produced by the negative action of $CHCl_3$. And its results have to be considered in the complex state of $CHCl_3$-narcosis, of which one of the components is discoloration of the blood.

The action of $CHCl_3$ is thus associated with the normal colour and with discoloration of the blood. With regard to the latter, the following fact is of value in the investigation of $CHCl_3$-action.

$CHCl_3$-vapour displaces a certain volume of air. The $-OXy$ atmosphere is associated with a certain degree of duskiness, which is measured by X. Now, when $CHCl_3$ is present in a moderate degree of overdose, and there is no mechani-

cal obstruction in the air-way,—the conditions being such that a respiratory overdose is prevented (*i.e.*, there is as free communication as the $CHCl_3$-air atmosphere allows of between the outside and the alveoli),—it will be found that the degree of duskiness, instead of corresponding to X—viz., the amount of air displaced—is X+Y, and that it increases proportionately with an increase of the overdose. This fact shows the importance of, I., differentiating between degrees of a result, and II., determining whether the degree of it under consideration is correspondent to the cause assigned to it. For the result may be (not a simple product, as is assumed, but) a complex one. Thus in the case of duskiness, one of the components of the state of $CHCl_3$-narcosis, the inference is drawn from the observations that have just been recorded, that two causal factors cooperate to produce it.

§ 40. *The amount of $CHCl_3$ necessary for Anæsthesia determined by the quantity and quality of the blood.*—Experience shows that the same amount of $CHCl_3$ is associated with different degrees of results in different individuals; and conversely that, in order to produce the same degree of result, *e.g.*, anæsthesia, different quantities of $CHCl_3$ are required by different indi-

viduals. Thus, assuming normal conditions and normal $CHCl_3$, and that there is no undue interference with the application of the graduated method, ʒss. is required by an infant of one year, ʒii. by a child of twelve, ʒiiiss. by an adult, and ʒii. by a man of eighty, for the purpose of inducing anæsthesia. The requisite amount of $CHCl_3$ increases with the age of the individual up to a period between 25 and 45, after which it begins to diminish. But it is to be noted that though these amounts are used they do not represent the amount absorbed into the blood. This is less than the quantity administered by the amount lost through evaporation, which is made constant by the successive application of comparatively small amounts at frequent but regular intervals.

In the case of the anæmic, the normal dose becomes excessive—*i.e.*, instead of anæsthesia, it is associated with narcosis. The normal dose has therefore to be reduced, and the amount of reduction is determined by the degree of anæmia.

Hæmorrhage may have occurred before, or may take place during, the operation. In severe instances, not only the quantity lost—viz., absolute diminution in the volume of blood—but also its result on the functions of respiration and circulation, which become depressed, thus leading to

a relative diminution in the volume of blood in the systemic circulation, have to be considered in relation to the amount of $CHCl_3$. For it is the actual quantity of blood at the time in the systemic circulation which determines it.

Fall in blood-pressure may occur in the course of $CHCl_3$-anæsthesia, primarily from reflex stimulation of the vaso-motor centre, or secondarily, through stomachic-inhibition of the respiratory centre. It varies in degree. And each degree determines a proportionate reduction of $CHCl_3$.

External hæmorrhage and vaso-motor depression are, in their relation to $CHCl_3$, illustrated by the following examples:—

I. $CHCl_3$ was administered to a healthy adult woman, *ætat.* 28. The maximum proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere needed to induce anæsthesia was 5 drops. Two days afterwards, in consequence of severe hæmorrhage, anæsthesia was again necessary. The pulse was 110 at the beginning of the second administration of $CHCl_3$. The maximum proportion was found to be 2 drops. Soon after the onset of anæsthesia, the frequency of the pulse fell to 90, thus showing that two causes had been in operation to accelerate it, and that the result of one disappeared in the course of

$CHCl_3$-action—viz., of emotional disturbance on the suspension of the functions of the mind.

II. In the course of $CHCl_3$ anæsthesia pallor occurs coincidently with pressure on an inflamed part of the intestine. The pulse is diminished in strength and increased in frequency. Before the circulatory variation the maximum atmosphere had been reduced from 5 to 4 drops. The degree of the variation required the reduction of the amount of $CHCl_3$ to 1 drop. At the end of 5′, the results of the complication had disappeared, and the proportion of $CHCl_3$ was raised to the maximum of 4 drops—*i.e.*, adjusted to the return of the normal volume of the blood to the systemic circulation.

III. $CHCl_3$ was administered to a youth soon after the occurrence of injury. The induction of anæsthesia was normally effected by a maximum of 3 drops. In the early stages of it respiratory inhibition and pallor supervened. The amount required to maintain the state of anæsthesia, under these abnormal conditions, was 1 drop. At the end of about 5′ the act of vomiting took place, after which the respiratory and circulatory systems returned to normal conditions, when the proportion of $CHCl_3$ was again raised, not to the initial maximum of 3,

but to 2 drops, in accordance with the law of diminishing resistance. Hence the mere occurrence of pallor does not necessarily signify that the action of $CHCl_3$ is to be temporarily withheld, but that its proportion in the mixed atmosphere is to be equated to the independent variation of the condition of the part which it affects.

In examples of initial $+CO_2$ condition of the blood, it is found that less than the normal amount is required to induce unconsciousness, and that this amount varies inversely with the degree of the abnormality. In diphtheria, therefore, comparatively small quantities are required. And it is important to note in these examples the improvement which takes place in the breathing during the administration of an atmosphere containing less than the normal proportion of oxygen. It is explained by the relaxation of the contracted muscles of the larynx.

In a case of laryngeal obstruction (male, *ætat.* 45), the proportion of $CHCl_3$ needed to induce mixed unconsciousness was 3 drops. After the completion of tracheotomy, and the establishment of normal aeration, the amount required for the purpose of maintaining anæsthesia was 6 drops.

From these examples the following conclusion is drawn—viz., there is a relation between the physiological action of $CHCl_3$ and the blood. The question then arises, Is this relation a fundamental one? And until this is answered it follows obviously that the conclusion will hold only a subsidiary position in the solution of the $CHCl_3$-problem.

§ 41. *The law of diminishing resistance.*—In the course of $CHCl_3$-action, it is found that when its proportion in the $CHCl_3$-air atmosphere is continued constant, there is a progressive increase in the degree of its results. And in order to maintain the constant state of anæsthesia, it is found necessary to progressively diminish the amount of $CHCl_3$. Thus, anæsthesia being induced and maintained in a normal adult for a period of 8′, at the end of it the amount of $CHCl_3$ is reduced from 6 to 5 drops, and this reduced proportion is continued for 10′, after which it is further reduced to 4, and so on, the interval between successive reductions increasing as the amount diminishes. But it is observed that constancy of condition does not characterise all the components of the state of anæsthesia, but only the degree of unconsciousness, as measured by the contracted pupil.

What is it that opposes a diminishing resist-

ance to the continued action of $CHCl_3$? Three data are involved in the solution of this question. They are the action of $CHCl_3$, the brain-centres, and the blood. It may be assumed that $CHCl_3$ affects the vitality of the centres. In support of this view, the long-continued period of unconsciousness, following upon the higher degrees of narcosis after the discontinuance of the administration, may be adduced. But $CHCl_3$-narcosis is associated with increased muscle-relaxation. The base of the tongue undergoes a greater degree of displacement than normally, and as a result produces a greater degree of mechanical obstruction in the air-way. But the normal patency of the air-way is one of the conditions that determine the quickest return to consciousness; for it is found that the length of the interval between unconsciousness and consciousness depends upon, 1, the degree of narcosis at the end of administration; and, 2, the degree of mechanical obstruction. The assumption, then, that $CHCl_3$ exercises only a direct action on the cerebral centres, is not in agreement with the evidence. For the $+CO_2$ factor, a remote $CHCl_3$-result, is known to be associated with suspension of the mental functions, and in certain circumstances may determine its prolongation after

the removal of its chief cause. Thus $CHCl_3$ appears to have a double relation to the cerebral centres, one direct, which is assumed, and the other indirect. It is essential to remove the indirect, so as to exclude the possibility of confusing them with direct results.

The argument against direct $CHCl_3$-action is supplied by the variations of the degree of unconsciousness accompanying variations of the proportion of $CHCl_3$, during the progress of anæsthesia. A slight diminution in the normal amount is immediately followed by change in the action of the respiratory machine, which becomes irregular—*i.e.*, associated with returning consciousness. The increase of the amount to the normal is, again, followed by immediate return to the condition of automatic respiration. On the other hand, if the normal proportion be slightly increased, the result is immediately manifested by a corresponding increase in the frequency of respiration and dilatation of the pupil. And the abnormal state thus induced immediately begins to return to the normal, on the reduction of the slight overdose to the normal proportion (which is determined by the "stage" in the course of anæsthesia at which the experiment is made). The result on the cerebral centres is inferred from, 1, the differ-

ence in the size of the pupil; and, 2, the length of interval that elapses before the return of consciousness after the administration ceases. Thus the cerebral centres are sensitive to slight variations in the degree of $CHCl_3$-action. Now, this sensitiveness opposes the assumption of direct action on the part of $CHCl_3$, for if comparison is made between drugs that are known to affect the mental functions directly and $CHCl_3$, this difference will appear, that while the state of functional suspension continues for some time after the direct agent has ceased to operate, in the case of $CHCl_3$ cessation of action is immediately followed by the beginning of the transitional return to consciousness.

These considerations lead to the suggestion of the indirect action of $CHCl_3$ on the cerebral centres, through changes in the blood, resulting in nutritional and functional disturbance.

The blood is dark in $CHCl_3$-narcosis. In $CHCl_3$-anæsthesia there is no apparent alteration in its colour. The part played by $+CO_2$ in the production of unconsciousness is secondary to that of another $CHCl_3$-factor. It cannot of itself initiate it, except under dangerous conditions of the respiratory machine; but it may assist in its causation. And it prolongs the stage of the return to consciousness. It is the

cause of increase in frequency of respiration. At the beginning of $CHCl_3$-anæsthesia, respiratory frequency is raised to 28. And in the progress of it there is a tendency to further increase, under the condition of a diminished amount of $CHCl_3$, and therefore of a larger proportion of air. If, with a relative increase in the volume of oxygen, which is normally associated with diminished frequency, there is increased frequency of respiration, it is clear that some other cause is present strong enough to neutralise its effect on the respiratory centre.

This cause is present and in operation at the commencement of anæsthesia. The frequency of respiration, 28, is thus not a simple but a complex result, due to the action of two causes, one of which—viz., the initial diminution in the proportion of oxygen in the atmosphere breathed—might be regarded as being the only cause present and in operation at the time of its appearance. But such partial treatment would inevitably introduce error into conclusions drawn therefrom—as that the displacement of air by $CHCl_3$ is the cause of all the increased frequency of respiration accompanying $CHCl_3$-action. The error can only be avoided by measuring the degree of the result, and comparing it with the quantity of the cause put forward to account

for it. Suppose, for example, some inert but respirable vapour takes the place of $CHCl_3$ in the normal $CHCl_3$-air atmosphere, will the displacement of an equal volume of oxygen by these two different agents be followed by the same increase in the frequency of respiration, if the conditions under which they act are the same? By inference from the facts above recorded, they will not. And thus $CHCl_3$ is shown to affect respiratory frequency in a twofold manner. One of these has already been isolated. The nature of the other remains at present undetermined. In favour of its indirect action, there is no stable connection between the physiological action of $CHCl_3$ and respiratory frequency, as is shown by the immediate and corresponding variations of the latter following upon slight variations in the proportion of the former.

To the sensitiveness of, I., the cerebral centres, and, II., the respiratory centre, may be added the attitude of the pupil, in order to illustrate the slight hold which $CHCl_3$ exercises on the tissues which undergo variations of their respective conditions in the course of its action.

In anæsthesia the pupil is contracted. In narcosis it is dilated. The size of the pupil is the measure of the degree of narcosis. A

variation of the proportion of $CHCl_3$ is immediately followed by a corresponding variation in the size of the pupil. Thus, upon an increase—and normal conditions are presupposed—the pupil begins to undergo a further degree of dilatation, but it does not reach the final degree of it until after an interval, during which the conditions of the blood and the respiratory machine are being equilibrated to the new condition of the $CHCl_3$-air atmosphere. So, upon a diminution of the amount of $CHCl_3$, the pupil immediately begins to contract, and, after a period of transition, finally reaches the lower degree of dilatation corresponding to the lower degree of $CHCl_3$-action.

The result of these experiments points very strongly in favour of the indirect action of $CHCl_3$. And in the process of isolating the intermediate cause, the known fact that the resistance of some part diminishes in the course of $CHCl_3$-unconsciousness may possibly be of assistance.

§ 42. *The intermediate cause.*—The problem is simplified by grouping these experimental results and relating them to a common cause, the product of $CHCl_3$-action. But an apparent difficulty is presented by the relation of the pupil to the state of unconsciousness. For, as

the degree of $CHCl_3$-unconsciousness increases, so in proportion does the size of the pupil increase. Is the pupil, then, governed by the condition of the cerebral centres?

In the two different degrees of unconsciousness, supplied respectively by sleep and opium-narcosis, the pupil is contracted. In the same degree of unconsciousness (as measured by the degree of cyanosis, supposing that it is an efficient gauge) the pupil is dilated when $CHCl_3$ is the cause, and contracted in the case of opium. It appears, therefore, that there is no direct connection between the pupil and the cerebral centres. In $CHCl_3$-narcosis, the condition of the former is thus independent of that of the latter.

A real difficulty, however, is encountered in the mechanism of the dilatation of the pupil. For it is a concomitant of the higher degrees of $CHCl_3$-action, and is, further, a separate phenomenon—*i.e.*, it is not dependent on any of the phenomena accompanying it. The pupil is dilated through fear, and by means of certain agents—*e.g.*, Atropin. Dilatation of the pupil is associated with, 1, the later stages of asphyxia; and, 2, sudden fall of blood-pressure. The structure of the iris is highly vascular, and its muscle-constituent is differentiated

from other involuntary muscles by the non-existence of nerves. Now, it is necessary to explain all the phenomena occurring in $CHCl_3$-action in order to arrive at the true solution of the problem, otherwise there is the probability of leaving out of the investigation the principal phenomenon. And it has yet to be disproved that the dilated pupil is not fundamental.

These two data—the diminishing resistance of some part affected by $CHCl_3$ and the causation of dilatation of the pupil—will thus assist in the work of discovering the intermediate cause. Inasmuch as they imply the existence of tendencies which are invariably associated with the action of $CHCl_3$, they form the proper sphere of its investigation rather than the occasional "convulsion," and the irregular phenomena which may complicate the functions of the circulation and respiration respectively.

§ 43. *Origin of irregularities occurring during $CHCl_3$-action.*—The initial conditions presented by the respiratory machine and blood are variant. They occur in combinations, differing both in kind and degree, and, in conjunction with the effect of $CHCl_3$, are responsible for the resultant changes which take place in them. If two vessels contain different quantities of

water, but the same amount of soluble pigment be applied to each, two different degrees of the same colour will be produced. The effect of the pigment is the same in each, and is proportioned to its amount, but it is associated with a difference in the result, determined by the difference which obtains between the two quantities of water. If, now, we substitute $CHCl_3$ for pigment, and blood for water,—for whatever the qualitative action of $CHCl_3$ may be, there is a quantitative relation between it and the blood,—we shall perceive that the effect of the same amount of $CHCl_3$ is always the same, and that differences, when they appear in the results, are to be ascribed not to the irregular action of $CHCl_3$, but to their proper source, which is the abnormal condition of the blood.

The conditions of the respiratory machine and the blood also vary during the progress of $CHCl_3$-unconsciousness. There are tendencies respectively to increased frequency of respiration, to mechanical obstruction by displacement of the base of the tongue,—a remote $CHCl_3$-result,—and to exhaustion of the respiratory muscles, arising from their increased activity. But besides these variations, which are de-

pendent on $CHCl_3$-action, other variations independent of $CHCl_3$ may appear and tend to divert the path of investigation from its proper channel.

A survey of the initial conditions of the respiratory machine and blood will lead to the detection of abnormalities if they exist. These are to be measured, and the particular details of the method — viz., the maximum amount and the rate of increasing the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere up to it—modified so as to meet their respective requirements. And thus irregularities from this source, viz., abnormal conditions, are made to disappear.

But it may happen that the initial abnormality is ignored on account of the moderate degree of its intensity. In this contingency, the advantage of familiarity with the normal progress of phenomena during the period of the induction of anæsthesia under normal conditions will become obvious. Let us suppose that there is a deviation from the normal, and that it is observed soon after its beginning. Its cause is at once ascertained, and the requisite means employed to put it out of action. Thus the state of complication is treated when

it is easily manageable. But let us suppose, on the other hand, that it is not detected before it reaches the later stages of its progress, where it assumes a less or greater degree of gravity,—not only will the complication be less easily manageable, but remote results also appear during its progress which are not properly the results of $CHCl_3$, but are mistaken for such. The following example illustrates the consequences of this error.

$CHCl_3$ was administered to an apparently healthy man of 65 by the normal method. At the end of 1′ duskiness was observed. The proportion of $CHCl_3$ in the CHC_3-air atmosphere had reached 3 drops, and this was immediately reduced to 2, in order to counteract the tendency to respiratory overdose, which it was supposed was beginning to be effective. But instead of an amelioration, the complication presented signs of increasing in intensity with undue rapidity, as shown by the rapidly increasing degree of duskiness. Now this result is contrary to experience derived from normal conditions, and hence suggested some abnormal condition. $CHCl_3$ was consequently withdrawn, and a gag placed between the teeth. But despite the partial removal of mechanical obstruc-

tion, duskiness continued increasing in degree, and respiratory movements became limited to the abdomen. The pulse, which had been diminished in frequency and increased in strength, now became rapid, and its subsequent disappearance was followed by general muscle-rigidity, which had been anticipated. Associated with this condition is displacement of the base of the tongue, and in order to be able to command the glottis, the mouth had previously been partially opened. The base of the tongue could then be easily placed in its normal position and maintained in it. And upon this procedure the gradual recovery of the respiration and pulse began. It was subsequently discovered that the abnormal condition was atrophic emphysema of the lungs. The fault committed was the relative rapid increase in the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere. The remote result of the complication is complete mechanical obstruction, preventing communication between the alveoli and the air, and thus becoming, if uncounteracted, the source of erroneous inference. The abnormal lungs being unduly sensitive to variations in the proportion of oxygen, become rapidly congested, and require a longer interval

than normal ones do in which to unload. To this end the patency of the air-way is essential; and it is easy to see that some time will be lost, and consequently some danger run, if any difficulty be encountered in separating the jaws. And such will be the case if the muscles of the lower jaw are rigidly contracted.

PART II.

THE $CHCl_3$ FACTOR.

§ 44. *Subdivisions.*—The study of the $CHCl_3$-factor includes, 1, its quality; 2, physical attributes; 3, spheres of action; and 4, the phenomena associated with its physiological action.

§ 45. Quality of $CHCl_3$. A tendency to decompose, under certain conditions, renders $CHCl_3$ an unstable fluid. These conditions are exposure to light, variation of temperature, and contact with air. To counteract this tendency, $CHCl_3$ should be kept in a dark place, at a constant temperature of 60° Fahr., and in relatively small bottles. By means of the last restriction, the influence of "contact with air" is reduced to a minimum, provided that $CHCl_3$ is in frequent use.

As the result of decomposition it becomes inferior in strength, and in consequence thereof its power as an anæsthetic agent is reduced.

The first essential, before the commencement of its administration, is therefore the knowledge that it is of standard strength. This is obtained through the sense of smell. And discrimination of differences in the characteristic odour of $CHCl_3$ is acquired by practice.

The use of $CHCl_3$ of inferior strength leads to erroneous inferences.

In a $CHCl_3$-air atmosphere, with standard $CHCl_3$ at the maximum, the corresponding volume of displaced air may be represented by x. If, instead of being of standard, the quality of $CHCl_3$ is of inferior strength, it will be found necessary to increase the normal maximum—from 6 to 8 or 10 or more drops—in order to produce unconsciousness. But with the increase in the proportion of $CHCl_3$ there is a corresponding increase in the volume of displaced air, which may be represented by $x+y$. Now, the difference between x and $x+y$—viz., the additional amount of displaced air—may be adjusted by a normal respiratory machine without undue obstruction to the function of aeration. But it does not necessarily follow that an abnormal respiratory machine shall be able to effect the adjustment within the same limits of least disturbance. For interference with the function of aeration directly leads to pulmonic conges-

tion. The congestion of normal lungs, up to a certain degree, is readily reducible, given a normally patent air-way, but is delayed when the air-way is obstructed at any point. If, however, the lungs are initially abnormal, in respect that the alveolar circulation is deficient, as, *e.g.*, in emphysema, it is clear that the same reduction in the normal proportion of oxygen in the alveoli will be followed by a relatively greater degree of disturbance than in the case of the normal alveolar circulation, and therefore that the degree of pulmonic congestion will be greater. The proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere determines the degree of pulmonic congestion. A large dose of inferior strength, rapidly administered, will be followed by rapidly increasing pulmonic congestion; administered by the graduated method, the same degree of congestion may be induced, but with less rapidity. The danger of pulmonic congestion resides, not so much in its actual degree, which, of course, must not transgress the extreme limit of safety, as in the maintenance of it over an undue interval of time. The degree attained may be extreme, but provided that air is in the alveoli, and is efficiently replaced, the obstruction in the alveolar circulation will be gradually reduced,

and thus relief given to the over-distended right ventricle.

The use of $CHCl_3$ of inferior quality brings into the foreground its negative action. The results induced by it are not "pure"—*i.e.*, the pulse, the frequency of respiration, the blood, and the cerebral centres are affected by two agents, viz., the physiological action of $CHCl_3$ and $+CO_2$. The kind of unconsciousness produced is thus not simple as in $CHCl_3$-anæsthesia, but mixed. And from its uncertain composition false conclusions may be drawn. Thus automatic respiration implies the condition of unconsciousness. But consequent upon the skin-incision a moan is audible, which may be accompanied by movement. There has been a temporary return to consciousness, the $+CO_2$ factor being, on supposition, in the larger proportion, and therefore responsible for the unstable character of the condition of the mental centres. But the temporary return may be, and is when the circumstances are favourable, followed by unconsciousness. The moan and movement are not, therefore, to be always taken as necessary indications for increasing the amount of $CHCl_3$. They are so only when the return to consciousness is continuous.

Let us suppose, however, that the proportion

of $CHCl_3$ is increased. What will take place? The rapid arrest of the action of the respiratory machine. The explanation is that the induction of unconsciousness by $CHCl_3$ of inferior strength is invariably associated with pulmonic congestion, which is continued after unconsciousness has been attained. If, under these abnormal conditions, the proportion of $CHCl_3$ is raised in the air-way, where it is already present in excess, but the effect of which is partially counteracted, the foundation of an absolute respiratory overdose will be laid, and respiratory overdose eventually becomes, if it is not uncounteracted, the chief factor in the causation of respiratory arrest.

From the use of $CHCl_3$ of inferior strength there arises the notion of the susceptibility of certain patients to its action. This is true, but not in the sense in which it is put forward. For there are two variants which are in question —viz., I., the quantity and quality of the blood; and II., the actual amount of $CHCl_3$, which varies according to its strength and the quantity used. Thus a large amount of inferior quality may have but little positive effect on a normal adult, whereas a comparatively small amount of standard $CHCl_3$ may produce dangerous results in the anæmic. If, on the other hand,

the maximum proportion of standard $CHCl_3$ in the $CHCl_3$-air atmosphere is equated to the quantity and quality of the blood, "susceptibility" disappears.

The fundamental requisite in $CHCl_3$-administration is the minimum displacement of air. This is achieved by the use of small amounts of standard $CHCl_3$ frequently administered. The proportion of $CHCl_3$ and the volume of air in the mixed atmosphere thus become practically constant during any one period in the course of anæsthesia; and as the consequence of the adoption of this plan, the detection of changes following upon slight variations of the amount of $CHCl_3$ is made possible.

If the proportion be gradually but unduly increased, a state of absolute safety will ultimately be converted into one of imminent peril. But this is not an argument against the use of standard $CHCl_3$: it is nothing more or less than evidence of a blood-overdose in a particular instance. A complication has been induced by an overdose of standard $CHCl_3$; it is remedied by reducing the amount of the overdose to the normal proportion. So in the case of the induction of unconsciousness, with excessive quantities of standard $CHCl_3$ there is a greater

displacement of air than is necessary. In all cases there results some degree of interference with the function of aeration, as is shown by the appearance of duskiness. But the consequences of this interference are not of the same degree in all states of the respiratory machine. For occasionally they reach a high degree of intensity, as, *e.g.*, in those examples in which some abnormality is present. Thus, the abnormal $CHCl_3$-air atmosphere tends to discover weak points in the respiratory machine. But instead of the complex state thus induced being analysed into its simple components—viz., that due to the effect of $CHCl_3$ and that to the influence of abnormal conditions as it should be—it is assumed to be simple, and in consequence the whole result is improperly ascribed to $CHCl_3$-action, and made the basis of an argument in favour of the artificial dilution of standard $CHCl_3$. The argument is valid for this exceptional instance, inasmuch as there is an excess of $CHCl_3$-vapour in the air-way, and therefore, by implication, an abnormal diminution in the proportion of air. It does not thence follow, however, that it is valid for uncomplicated examples. But in the place of air, which is the natural diluent of respirable vapours, other agents, such as ether, alcohol,

&c., are introduced which, in the form of vapour, equally with $CHCl_3$ displace air. Thus $CHCl_3$ is diluted, but without increasing the proportion of air in the compound atmosphere; and thus the end-object, which is the counteraction not of the physical but of the negative action of $CHCl_3$ and its associates, is defeated.

The use of $CHCl_3$ of inferior quality may be accompanied by just as many difficulties, and be the source of as much perplexity, as that of standard strength when its proportion is abnormal and its administration irregular. It supplies one of the reasons for the notion of the (comparatively) large amounts required for the purpose of inducing unconsciousness. It explains, in part, the irregularities which are associated with $CHCl_3$-action, and the inferences drawn therefrom. As thus: it may chance that a given quantity below the standard strength, administered by a method which, though not normal, is yet supported by the results of experience, exactly agrees with the requirements of a few individuals presenting more or less like conditions of the respiratory machine and the blood. The inference is then drawn from a limited number of instances that the quantity which is found to be normal for some will be so for all. But a widening of experience shows

that that amount is too large for this and too small for that one, and may occasionally be accompanied by exceptional phenomena. The soundness of the conclusion will therefore be open to criticism. And in order to explain the variations appearing in the results obtained, their origin is erroneously ascribed to the irregular action of $CHCl_3$, instead of being derived, as it really is, from one or more of three variants—viz., the quality of $CHCl_3$ and the abnormal conditions of the respiratory machine and of the blood.

§ 46. *The physical attributes of* $CHCl_3$.—There is no obvious manifestation of any local action of $CHCl_3$ on the mucous membrane of the respiratory tract when it is administered normally, diluted with air. But if $CHCl_3$-vapour be concentrated and projected upon the same area of the oral mucous membrane, as it is by fixing the issuing tube of Junker's apparatus to the gag, the surface will become blanched, and loss of sensation in it continue for some time after the return to consciousness. These untoward consequences provide an argument against the fixed position of the tube.

When cough occurs, as it may do in abnormal conditions of the lungs, it is due to temporary disturbance in the alveolar circulation.

Each case requires more $CHCl_3$ in summer than in winter, on account of the greater waste through evaporation. Consequently undue evaporation determines a shortening of the interval between the application of successive increments of $CHCl_3$, in order to obtain a practically constant $CHCl_3$-air atmosphere. Loss through evaporation, in cases where the addition of $CHCl_3$ is not related to the inhibited or temporarily arrested action of the respiratory machine, explains the large quantities used, apparently without effect. For a full inspiration is postponed until the vapour is sufficiently attenuated. The rational course in all these instances is to allow the blood, which is more or less deoxygenated as the result of inhibited or voluntarily arrested breathing occurring in the course of induction, to become sufficiently oxygenated before proceeding with $CHCl_3$. But after an inspiration of air the breathing may be again inhibited (or arrested, as is frequently the case in infants). The difficulty arises either from an initial overdose, or from not timing the inspiration—*i.e.*, the increment of $CHCl_3$ is to be added immediately before its anticipated occurrence.

But it is in the density of its vapour that the chief importance of $CHCl_3$, physically con-

sidered, resides. A heavy vapour tends to descend in a closed cavity. Now, the lungs become a closed cavity when respiration is arrested and the air-way obstructed at the glottis. Should these conditions obtain, and delay occur in the removal of the source of obstruction, $CHCl_3$-vapour will descend in the meanwhile. It follows, therefore, that after the obstruction is finally removed, a longer interval will be needed for the artificial expulsion of the contents of the air-way. Thus the length of the delay has an important relation to subsequent recovery.

The action of the respiratory machine naturally adjusts itself to slight alterations in the weight of the mixed $CHCl_3$-air atmosphere. If the latter be gradually increased, the former will continue to manifest a tendency to adjust its action to the varying condition, but with increasing inefficiency, and only for a definite period, by reason of the limited resources of its motor-power. If, however, the increase in the proportion of $CHCl_3$ is more or less rapidly effected, the favourable condition to increased activity of the respiratory machine—viz., the gradual accumulation of $+CO_2$—is absent. The heavy mixed atmosphere being opposed by a respiratory force which is incapable of efficiently

expelling it, thus becomes the determining factor in the causation of respiratory arrest.

An excess of $CHCl_3$-vapour in the air-way—*i.e.*, a respiratory overdose—is absolute when the initial amount is an overdose. Its operation may be assisted, during the period of induction, by voluntary inhibition or arrest of respiration. And its result is manifested by the rapid disablement, terminating in the temporarily arrested action, of the respiratory machine.

If the initial amount is normal, a relative respiratory overdose will follow upon, 1, mechanical obstruction in the air-way; and, 2, voluntary inhibition of respiration during the period of the induction of unconsciousness. But there is this difference regarding treatment between an absolute and a relative respiratory overdose. In the former the weight of $CHCl_3$-vapour is not immediately reduced to a sufficient degree by simple diffusion, consequently the artificial expulsion of the abnormal contents of the air-way becomes necessary. But in the latter it is controlled, and its degree is sufficiently reduced by diffusion, to allow of the manifestation of respiratory activity. The progress of the abnormal phenomena accompanying a relative respiratory overdose is obviously less rapid than that of an absolute one. And it will be per-

ceived that a comparatively long interval, in which deviation from the normal course may be detected, is of importance in practice. In the course of normal anæsthesia, a relative respiratory overdose occurs when the air-way is obstructed, or when the action of the respiratory machine is either inhibited by stomachic disturbance or accelerated as the secondary result of stimulation of the vaso-motor centre. The treatment of the relative respiratory overdose consists in removing the predisposing factor, as in the case of displacement of the base of the tongue; or where this is impossible, as in stomachic inhibition and vaso-motor depression, in regulating the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere to the requirements of the abnormal condition of the respiratory machine.

§ 47. *The spheres of $CHCl_3$-action.*—$CHCl_3$-vapour displaces air, and consequently interferes with the function of aeration. This is its negative action. When present in excess in the air-way, its weight opposes an abnormal resistance to the muscles of expiration. This is its physical action. It is absorbed into the blood, and is associated with certain phenomena. The set of phenomena or the state is the manifestation of its physiological action.

These different kinds of action may be present

in all possible combinations. Thus the negative and the physiological; respiratory overdose and the physiological; the negative and respiratory overdose; or all three may operate simultaneously. And each kind may also present differences in the degree of its intensity. Thus the degree of the negative action may be greater or less than that of the physiological. It becomes necessary, therefore, to differentiate between the complex states which result respectively from the predominance of either of these causal factors, in order to avoid confusing the results of the one with those of the other. The means of differentiation exists in the attitude of the pupil. The pupil is contracted when the $+CO_2$ factor (*i.e.*, the negative action) is in the ascendant; it is dilated, and tends to lose its sensitiveness, when $CHCl_3$ is acting chiefly physiologically. True knowledge of causation leads to the explanation of apparently irreconcilable results. The $+CO_2$ factor is associated with pulmonic congestion. It is, consequently, in indirect association with cardiac variations. And it is known to be directly associated with stimulation of the respiratory centre. A cause is thus at hand to account for differences in the frequency of the pulse and of respiration. Further, pulmonic congestion, when the cir-

cumstances are favourable to their occurrence, is followed by exhaustion of the respiratory muscles and cardiac syncope. It is of fundamental importance, therefore, in the investigation of the causation of results, to indicate the sphere of $CHCl_3$ action from which they take their origin.

The physical action of $CHCl_3$ may be more or less rapid. The rapid occurrence of respiratory arrest has been causally associated with the direct action of $CHCl_3$ on the respiratory centre. Now, it is true that a respiratory overdose of sufficient intensity directly prevents the manifestation of the action of the respiratory machine. But is it also true that $CHCl_3$ causes respiratory arrest by its depressant influence on the respiratory centre? The action of $CHCl_3$ is in fact associated with respiratory arrest in certain circumstances. But in each instance it is necessary to indicate the sphere of its action. Thus, it may either be in the air-way, a direct result of its physical action; or in muscular exhaustion, an indirect result of its negative action; or, again, it may be assumed to be the respiratory centre. But instances occur of arrest of the function of centre during $CHCl_3$-action, but which are not causally associated with it; and in consequence an ele-

ment of perplexity was introduced into the solution of the problem. For the question proposed was not, What is the particular cause in each instance? but, What is the common cause in all instances of respiratory arrest? And the answer was given in favour of the depression or paralysis of the respiratory centre, which was caused by the action of $CHCl_3$ on it. The error arose from, 1, arbitrarily circumscribing the sphere of $CHCl_3$-action; and, 2, deriving the wrong cause in those instances of reflex arrest of the action of the respiratory centre. Thus, in order to arrive at the phenomena which are associated with its physiological action, it is essential to exclude, I., undue degrees of intensity both of the negative and the physical action of $CHCl_3$; and, II., the action of independent causes. But an initial difficulty is presented by the fact that there are different degrees of that action that are determined by the different proportions of $CHCl_3$ in the $CHCl_3$-air atmosphere. The lowest degree associated with unconsciousness is termed the anæsthetic; and the degrees above this are called narcotic, the actual degree of these latter being measured by the degree of dilatation of the pupil. In the state of anæsthesia there is no abnormal interference with the function of aeration. But in

that of narcosis there is of necessity (for the respiratory machine is selected by common consent as the vehicle for conveying $CHCl_3$ to the blood, and its action is subservient to the function of aeration) less or greater interference with that function according to the less or greater displacement of air. Constancy in results, therefore, will be maintained, but only for a definite period of time, by preserving a constant relation between the excess of $CHCl_3$-vapour and the diminished volume of air. The state of narcosis, however, is complex, and should not be regarded as representing simply the physiological action of $CHCl_3$, but as the resultant of its negative and physiological actions, of which the latter is the chief. The variations of pulse and respiratory frequency, which are induced by the combined effects of these two actions, are therefore not pure results. Thus the pulse, let us suppose, is beating at 60 in $CHCl_3$-narcosis. In $CHCl_3$-anæsthesia, the pulse-frequency is slightly accelerated—viz., 73. The physiological action of $CHCl_3$, without its negative action, is associated with slight stimulation of the cardiac function; but with its negative action it is associated with a diminution in the frequency, but at the same time with an increase in the strength, of the heart's

contractions. These two different degrees of action, therefore, in this respect oppose each other. But the negative action is known to cause a reduction in the cardiac frequency. The question then remains, Is the whole of the reduced frequency caused by negative action? If it is not, it follows that some portion of it is the result of physiological action. But that conclusion—and it is to be observed that it is assumed, and will remain so, until it has been proved how physiological action reduces cardiac frequency—leads to the following contradiction. The anæsthetic degree of the physiological action of $CHCl_3$ increases the pulse-frequency slightly. The narcotic degree diminishes it to an extent which varies according to the amount of the overdose. Increased cardiac frequency implies stimulation. And the results of stimulation increase, with an addition to its source, up to a certain limit. But there is no evidence to show that this limit has been exceeded in the present instance, because, as the terminal result of stimulation, exhaustion supervenes quickly when the initial degree of stimulation is intense, more or less slowly when it is moderate and prolonged over an interval of time, whereas, during this assumed physiological action of $CHCl_3$, the heart instead of losing increases in strength.

But not only is the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere to be maintained constant, but also the air-way is to be kept normally patent if we are to obtain $CHCl_3$-results free from contamination with the products of slight degrees of mechanical obstruction. For this abnormal condition becomes a cause, the action of which complicates some of the results which are associated with $CHCl_3$-action—viz., respiratory frequency, condition of the lungs, colour of the blood, and frequency of the pulse.

§ 48. *The phenomena associated with the physiological action of $CHCl_3$.*—To obtain these results the following requisites are necessary: 1, $CHCl_3$ is to be brought into relation with the blood without any other complication of the respiratory machine than that due to its negative action, which, in the case of the anæsthetic degree, is reduced to a minimum, and practically disappears; 2, the initial conditions of the respiratory machine and the blood are to be normal; and 3, the air-way is to be maintained normally patent throughout the period of unconsciousness in which records are taken.

Automatic respiration is the fundamental sign of the state of unconsciousness—*i.e.*, the suspension of the functions of the mind. But the

degree of disturbance in the cerebral centres, resulting from $CHCl_3$-action, varies according to the degree of that action. The state of unconsciousness is thus not one and the same in all instances, but it varies in degree.

In anæsthesia the phenomena are—1, increased frequency of respiration; 2, efficient respiration indicated by normal oxygenation; 3, natural colour of the complexion (no apparent alteration in the colour of the blood); 4, normal condition of the venous system; 5, slight increased frequency of the pulse; 6, contracted or pin-point state of the pupil—the measure of the lowest degree of $CHCl_3$-unconsciousness; and 7, muscle-relaxation. It is important to note that the state of anæsthesia allows of the manifestation of reflex results when occasioned—*e.g.*, sensori-motor, vaso-motor, or stomachic inhibition of the respiratory centre, thereby showing that it presents but slight impediment, if any, to the transmission and reception of stimuli by the nerves and lower nerve-centres respectively.

If the same amount of $CHCl_3$, being the anæsthetic proportion for a given stage only, is continued beyond that stage, the phenomena, instead of remaining constant, undergo a variation. They slowly assume the characters which they present in the narcotic state. In the course

of this deviation from the normal, the following phenomena present the same proportionate degree of variation—viz., increasing activity of the respiratory machine, the dark colour of the blood, venous distension, and dilatation of the pupil.

In the course of the constant state of normal anæsthesia, effected by the progressive reduction in the amount of $CHCl_3$, the action of the respiratory machine continues efficient, the blood preserves its normal colour, and the pupil remains in the state of contraction. But a tendency to an increase in the frequency of respiration appears, and is followed by a corresponding increase in the frequency of the pulse. Besides these, there is a tendency to increase in the degree of muscle-relaxation, shown by the less ready response of the muscles to direct stimulation in the course of anæsthesia, as compared with their apparently normal sensitiveness at the commencement of it. Reflex actions, vaso-motor and stomachic inhibition, are apparently not effected; but in sensori-motor a stronger stimulus is needed to produce the same degree of contraction after the lapse of an hour which was effected at an earlier stage by a weaker one. Inasmuch as the condition of the muscles does not remain

constant, it is impossible to infer with certainty that there is any impediment, in the nerves or nerve-centres, to the passage of stimuli through them. But assuming that there is, it cannot be very considerable, seeing that in other varieties of reflex action there is no manifestation of delay in the transmission of stimuli.

In narcosis the phenomena are: 1, abnormal activity of the respiratory machine, associated with inefficient aeration, as shown by, 2, the discoloration of the blood; 3, acceleration of the frequency of respiration; 4, diminution in the frequency of the pulse, accompanied by an increase of its strength; 5, dilatation of the pupil; 6, comparative increase in the degree of muscle-relaxation; and 7, venous distension. And sensory nerve-stimulation is followed by a comparative decrease in the degree of muscle-contraction—the comparison always being made with the results obtaining under like circumstances in anæsthesia.

If the amount of $CHCl_3$ is unreduced, the degrees of these phenomena severally tend to increase with a rapidity the rate of which is determined by the degree of the initial overdose. But if the amount is reduced, but not to the normal, the same tendency appears, but in the opposite direction, after the conditions

of the respiratory machine and blood have become equilibrated to the diminished proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere—*i.e.*, after an interval there is a reduction of the degree of narcosis, which, however, is only constant for a definite period.

The degree of the initial overdose determines the degree of narcosis (as measured by the degree of dilatation of the pupil). A change in the former, whether of increase or diminution, is followed by the appearance of changes in the components of the latter respectively; and there is a direct proportion between them. Thus the variations of the respiratory machine, of the colour of the blood, the frequency of respiration and the pulse, the distension of the veins, and the size of the pupil, always preserve the same relationship to each other, increasing or diminishing in the same ratio.

If a comparison be instituted between the states of anæsthesia and narcosis, it will result in the detection of differences in the size of the pupil, the colour of the blood, the frequency of respiration, and the character of the pulse. But these differences do not indicate that $CHCl_3$ has different kinds of physiological action. For, first, an anæsthetic proportion of $CHCl_3$, if continued beyond its proper stage, will be followed

by commencing narcosis, which will increase unless the amount of $CHCl_3$ is reduced to meet the requirements of some changing condition or conditions; and, secondly, the displacement of air by an initial overdose has to be taken into consideration, as able to produce the whole or a part of some of the phenomena—viz., discoloration of the blood and increased frequency of respiration, which might otherwise be ascribed to the physiological action of $CHCl_3$.

The $+CO_2$ factor—*i.e.*, imperfect aeration—might be adduced to explain all the phenomena of the narcotic state, with the exception of the dilated pupil. Thus the acceleration of respiration is the consequence of stimulation of the respiratory centre by $+CO_2$ (or $-OXy$). The diminution in the frequency of the pulse and the increase of its strength is the result of pulmonic congestion,—an associate of the $+CO_2$ factor,—to which also is to be ascribed the abnormal action of the respiratory machine. And the tendency to increasing muscle-relaxation is explained by the continued interference with its normal blood-supply. But the dilated pupil of $CHCl_3$-narcosis remains outside the sphere of $+CO_2$-action, by reason of the following differentiating characters: 1, the degree of its dilatation is proportioned to the degree of the

overdose; 2, with progressive increase of the overdose the pupil dilates neither suddenly nor rapidly, but progressively; 3, as it dilates it tends to lose its sensitiveness. On the other hand, during the gradual or rapid accumulation of CO_2 in the blood, the pupil — as is demonstrated by those examples in which the state of anæsthesia is complicated by mechanical obstruction — remains contracted for a definite period of time, during which the respiratory movements, though laboured, are continuous. And it only dilates—but rapidly while at the same time preserving its sensitiveness—at the moment when the continuity of the action of the respiratory machine is temporarily interrupted by the proximate cause of the $+CO_2$ factor—*i.e.*, when the supply of air to the alveoli falls below the minimum limit consistent with the continuity, under abnormal conditions, of the alveolar circulation; and it contracts as rapidly as it dilates after the source of obstruction has been removed — *i.e.*, when a proper proportion of air reaches the alveoli.

§ 49. *Value of the contracted pupil.* — From automatic respiration — a secondary result of $CHCl_3$-action—and the normal colour of the blood, the contracted pupil may be inferred. But, given automatic respiration and the con-

tracted pupil, the inference does not necessarily follow that the colour of the blood will be normal. For the two phenomena, automatic respiration and the contracted pupil, may be associated with duskiness, the result of a collateral cause — viz., mechanical obstruction—which may or may not be dependent on $CHCl_3$-action. But this possibility does not detract from the practical utility of the contracted pupil as the measure of the anæsthetic degree of $CHCl_3$-action. Assuming $CHCl_3$ to be the only agent in operation, if the respiration be automatic and the pupil contracted or pin-point, it follows as a necessary consequence that the colour of the blood will be normal. But $CHCl_3$ may not be acting alone. It may happen that another cause co-operates with it, and that though they both affect some phenomena, thus rendering them complex, yet the pupil is unaffected by the complicating cause, and remains in the condition of normal contraction. The contracted pupil is thus seen to be a factor which is common to different sets of phenomena or states—*e.g.*, it is one of the components of $CHCl_3$-anæsthesia, and it is the only component which is unaffected when this state is complicated by mechanical obstruction. Again, the contracted pupil is present during

the early stages of returning consciousness, in which it is associated with diminished frequency and range of respiratory movements and normal colour of the blood. Lastly, it accompanies inhibited respiration and the lower degrees of fall of blood-pressure. Given automatic respiration, the inference drawn from the contracted pupil is limited to the anæsthetic (or safe) degree of $CHCl_3$-action under the conditions. It does not, therefore, necessarily include the normality or safety of those conditions—an error which is apt to be made when the attention is confined to the action of $CHCl_3$ alone, to the exclusion of a possible complicatory agent. The normal state of the patient as distinguished from the normal action of $CHCl_3$ can thus only be inferred from two data—1, the contracted pupil, and 2, the normal colour of the complexion.

The relation of the contracted pupil to $CHCl_3$-action may be secondary, through the suspension of the mental centres, and for this reason the degree of its importance as a factor in the solution of the problem cannot at present be estimated. But the relation between the higher degrees of $CHCl_3$-action and the dilated pupil is fundamental. Like the other components of the state of narcosis, its degree varies directly

with variations in the degree of narcotic action. Given initial normal conditions, and the maintenance of the normal patency of the air-way throughout the course of the experiments, the state of anæsthesia—contracted pupil, normal colour of the blood—is converted into that of narcosis—dilated pupil, dark colour of the blood —by increasing the proportion of $CHCl_3$. If the increase be effected by small and successive increments, the conditions of the pupil and the blood immediately undergo changes in response to each addition, becoming respectively larger and darker. If, now, corresponding reductions be made in the proportion of $CHCl_3$, at each stage the state of narcosis immediately begins to pass to a lower degree, as evidenced by the pupil becoming less dilated and the colour of the blood less dark. The return to the state of anæsthesia being supposed to be effected, if the proportion of $CHCl_3$, instead of being increased, is reduced by increments, the result of the change in the constitution of the $CHCl_3$-air atmosphere becomes immediately obvious in the diminished frequency of respiration and the reduced range of respiratory movements which are followed in the course of the reduction by irregular breathing and the dilatation of the pupil. At any stage in the return to conscious-

ness (up to the appearance of the dilated pupil) automatic respiration is restored by increasing the proportion of $CHCl_3$ to the normal. Thus, whatever its qualitative action may be, the results of these experiments show that the parts affected by $CHCl_3$ — and in the higher degrees of its action the pupil is one of them— are extremely sensitive to slight variations of the quantitative action. They establish what may be called the evanescent character of $CHCl_3$-action; and it may be added that though the degrees of disturbance induced respectively in the iris and blood may be high, they disappear on the withdrawal of $CHCl_3$ without leaving any apparent trace of damage to their functions.

The occurrence of dilatation of the pupil in the course of $CHCl_3$-action is of the highest practical importance. It may be the result of a blood-overdose of $CHCl_3$, absolute or relative. This kind of dilated pupil is dangerous. On the other hand, it may be the result of some cause independent of $CHCl_3$, but acting simultaneously with it. This kind is in itself innocent.

Thus, as in the case of the contracted, the dilated pupil belongs to different sets of phenomena. And its origin is likewise determined

by the phenomena which accompany it. But in doubtful instances it is prudent to regard it as a sign of danger, for it may be complex in its causation. If the whole or some part of it is due to $CHCl_3$-narcosis, the withdrawal of $CHCl_3$ will be followed by gradual in the former and rapid reduction to the degree of dilatation corresponding to the degree of narcosis in the latter. If $CHCl_3$-action be actually anæsthetic, its withdrawal in complicated cases will be followed by signs of returning consciousness, and these, of course, will determine its readministration, but with the necessary modifications in the details of the method. The consequences of mistaking the true nature of the dilatation of the pupil are seen in the subsequent arrest of respiratory movements in those cases in which accidental factors have been favourable to its occurrence. Thus, the initial state of the motor-power of the respiratory machine may be below the normal. But in $CHCl_3$-narcosis more work is done by the respiratory muscles than in $CHCl_3$-anæsthesia, and, therefore, than the normal amount. In these circumstances, the motor-power is not economised, and consequently its exhaustion will appear early. On the other hand, the initial motor-power may be normal, and the

duration of $CHCl_3$-narcosis may be prolonged beyond the customary limits. In these circumstances, the conditions will not remain the same.

A degree of narcosis which of itself is practically safe for a period of, say, half an hour, will become dangerous if its duration is extended beyond that limit. The reason for its becoming so is forthcoming in the change that takes place in the condition of the respiratory muscles. In the first period, that power is undiminished, and they are able to counteract, though with a decreasing degree of efficiency, the obstructant effect of the abnormal $CHCl_3$-air atmosphere; but afterwards they manifest the natural consequence of this abnormal activity — viz., exhaustion — by the increasing degree of insufficiency with which they endeavour to overcome an obstacle which is constantly opposing them. Under these circumstances rapid respiratory arrest occurs as a late phenomenon; or mechanical obstruction may intervene and determine sudden arrest of the action of the respiratory machine—complete obstruction at the end of inspiration—or hasten its onset—incomplete obstruction during $CHCl_3$-narcosis. The time of onset which, by reason of its irregularity, is adduced as proof of the

irregular action of $CHCl_3$, is thus in reality determined by the different kinds and degrees of all the abnormalities affecting the several components of the respiratory machine.

These instances have one common factor—viz., an abnormal state of the respiratory machine. The defect of respiratory arrest is traced to one or another or a combination of the components of this abnormal state. But arrest of respiratory movements occasionally occurs during $CHCl_3$-anæsthesia—*i.e.*, when the state of the respiratory machine is normal. Thus arrest of respiration occasionally takes place both during a normal and an abnormal state of the respiratory machine. And this circumstance might lead to the inference that the state of the respiratory machine is not of fundamental importance in the causation of the arrest of its action. But it can only do so by restricting "respiratory arrest" to a single source—viz., the action of $CHCl_3$ on the respiratory centre. Thus, the mere occurrence of arrest is hypothetically explained. But there are differences in the modes of its onset, and in the characters of the variations of the pupil accompanying it. As these differences are not explained by the hypothesis, it will be obvious that the functions of the latter have not been

completely fulfilled. Now it is these differences which supply evidence for the presence and operation of a cause (other than that of the assumed direct action of $CHCl_3$ on the respiratory centre) which may conceivably account for not only respiratory arrest, but also all the phenomena attending it.

The object, then, of analysis is to isolate the components of a complex state and the phenomena of each simple state. Suppose any cause in operation, it can only produce one set of phenomena, one of which is fundamental. But in two different sets of phenomena or states, the same phenomenon—*e.g.*, pallor—appears. It is of primary importance in one, of secondary importance in the other. The determination of its value will at once remove a source of perplexity. It is the same with respiratory arrest. And whether it is of primary or secondary value, is ascertained by the nature of the phenomena accompanying it.

But two or more causes may operate simultaneously, and all affect the same component either of the respiratory or circulatory systems. Thus, I., the pulse may be affected by, 1, the negative action of $CHCl_3$, causing indirectly diminution of its frequency and increase of its strength; 2, its physiological action, associated

with slight increase of frequency; and 3, moderate degree of vaso-motor depression, causing directly diminished strength and increased frequency. II., The frequency of respiration may be affected by, 1, the negative action of $CHCl_3$ causing indirectly stimulation of the respiratory centre; 2, mechanical obstruction to the air-way, acting in like manner; and, 3, reflex inhibition of the respiratory centre, the direct result of stomachic disturbance. Each of these results—viz., the condition of the pulse and respiratory frequency—may thus be complex. Supposing one of them to be so, and that it is ascribed to the action of $CHCl_3$ alone, without regard to the complexity of its condition, it follows that not only will error be introduced into the conclusion, but a fallacy will also be committed involving the causation of some subsequent variation of either of these phenomena, such as failure of the pulse or arrest of respiratory movements. The consequence of the fallacy may possibly be the exclusion of their principal causal factors respectively.

The result of isolating the action of a cause acting collaterally and simultaneously with $CHCl_3$ leads to the removal from the field of study—viz., that of the investigation of the physiological action of $CHCl_3$—of all the phe-

nomena not properly belonging to it. Some, not all, instances of respiratory arrest and pulse-failure are caused by $CHCl_3$. The question thus becomes confined to its natural limits, How may $CHCl_3$ produce respiratory arrest? Is its method of procedure always the same in all instances which are caused by it?

§ 50. *Summation of the sources of irregularity.* —$CHCl_3$ is a variant, in respect both of its strength and the degree of its action. The initial conditions of the respiratory machine and of the blood are also variants. The condition of some part, not at present isolated, undergoes a variation and offers a diminishing degree of resistance to the continued action of $CHCl_3$. Causes independent of $CHCl_3$ may occasionally intervene and complicate the state of anæsthesia or narcosis. Some of their results resemble, and may be mistaken for, those of $CHCl_3$.

To obtain a constant effect of $CHCl_3$, it is necessary to maintain the degree of its action constant.

To obtain the anæsthetic effect of $CHCl_3$, it is necessary to limit its action to the degree of anæsthesia. The anæsthetic degree is not constant for all cases, but varies with each. Thus different degrees of action are required to

produce the same anæsthetic effect in different instances.

To obtain constant results, two requisites are necessary: 1, constant degree of $CHCl_3$-action; 2, constant condition of the parts directly or indirectly acted upon.

To obtain normal results, it is necessary to limit $CHCl_3$-action to the normal or anæsthetic degree, and to exclude all abnormal conditions of the respiratory machine and of the blood. Thus the normal degree of $CHCl_3$-action upon normal conditions produces normal results—*i.e.*, the state of normal anæsthesia. But it is found that that state remains constant for a period only, and that to obtain a continuous constancy, it is necessary to progressively reduce the degree of $CHCl_3$-action. Thus the constant state of normal anæsthesia is isolated. By its means it becomes possible to study with accuracy the results of intervening causes.

PART III.

RESULTS.

§ 51. *Two stages in $CHCl_3$ administration.*—The transitional interval between consciousness and unconsciousness is called the stage of induction (of unconsciousness). Its characters vary according to the kind of method which is practised. The state of unconsciousness once attained, it is necessary to maintain it by the addition, at intervals, of $CHCl_3$. This is called the stage of unconsciousness. It varies in length according to the degree of $CHCl_3$-action, its duration, and the measures taken to promote the return to consciousness after the completion of surgical operations. When the action of $CHCl_3$ is limited to the production of the lowest degree of unconsciousness, *i.e.*, anæsthesia, the return to consciousness, and therefore to normal conditions of nutrition, is effected in the least possible time.

§ 52. *Method of administration.*—There can be no absolute uniformity in the results of any one method, for the reason that neither the respiratory machine nor the blood invariably presents respectively the same conditions. But there is a greater or less approach to it, according as a given method more or less agrees with the requirements of these factors. Thus, the normal method is associated with a manifest tendency to uniform results. If we differentiate between the individual instances, and call those which are precisely similar to one another, and occur most frequently, normal, and those which present some kind of dissimilarity, and occur less frequently, abnormal, then we shall find that the normal method is associated with absolute uniformity in (its normal) results. The absence of uniformity, when no differentiation is made between normal and abnormal conditions both of the respiratory machine and blood, is explained by the inclusion of the latter, which are in a minority, in a group to which they do not belong, and to the requirements of which the normal method is not adapted. The normal method is designed for, and its application consequently confined to, normal conditions. If applied to certain abnormal conditions, it will become, relatively to those conditions, a form of

the rapid method, and will be followed by characteristic results that are the outcome of it. But if, on the contrary, the details of the normal method be adapted to the particular requirements of each abnormality of both the respiratory machine and blood, anæsthesia will be normally induced. But the resulting state of anæsthesia will only be normal as to the contracted pupil and the normal colour of the blood. It will be abnormal as to the frequencies of the respiration and of the pulse, because the initial abnormality is one of their determinants.

The normal induction of anæsthesia is possible in all instances. But it can only be effected by the necessary adaptation of the principles which govern the administration of $CHCl_3$.

§ 53. *The Rapid Method.*—The end-object of $CHCl_3$ administration is the presence of $CHCl_3$-vapour, in proper proportion, in the alveoli. The principles which guide it are, 1, the gradual displacement of air by the correspondingly gradual increase in the amount of $CHCl_3$ up to the maximum, which varies in different instances; and 2, equating the amount of $CHCl_3$ to the quantity and quality of the blood.

Gradual displacement of air in the $CHCl_3$-air atmosphere prevents the feeling of suffocation

which is erroneously associated with the early stages of $CHCl_3$-action, and consequently will tend to restore confidence, if it be impaired, through the minimum degree of disturbance which is produced in the action of the respiratory machine, and consequently in the function of aeration. The gradual increase in the proportion of $CHCl_3$ ensures an efficient control over the weight of its vapour in the air-way: an undue degree of intensity of its physical action—*i.e.*, the occurrence of a respiratory overdose—is thereby avoided. Thus, excluding the normal proportion of $CHCl_3$ in the air-way, there is no obstacle to the passage of the $CHCl_3$-air atmosphere to the alveoli, and no impediment to the expulsion of the contents of the air-way.

But as the results of the Rapid Method—which was designed to produce unconsciousness as quickly as possible, in order to counteract the intermediate influence of volition—there follow, 1, rapid displacement of air; and, 2, an absolute excess of $CHCl_3$-vapour in the air-way, opposing, according to its degree, greater or less resistance to the act of expiration, and interposing an obstacle to the free communication between the external air and alveoli. As the consequence of respiratory obstruction, a

short interval occurs immediately before the onset of unconsciousness, during which the function of aeration is temporarily embarrassed. As the direct consequence of this embarrassment, CO_2 is rapidly accumulated in the blood, while oxygen is as rapidly diminished.

Rapid deoxygenation of the blood is associated with the early appearance of excitement and the late appearance of muscle-rigidity. The former is explained by disturbance to the nutrition of the cerebral centres consequent upon imperfect blood-supply; the latter, by the rapid diminution of oxygen in the blood supplying the muscles.

These results—viz., excitement and muscle-rigidity—invariably occur in the course of the rapid induction of unconsciousness, and form the basis of the division of this stage in the administration into three well-defined sub-stages: 1, that of excitement; 2, of clonic convulsions; and 3, of tonic spasm followed by stertor, muscle-relaxation, and unconsciousness. Of these, by far the greatest importance attaches to the second, viz., the sub-stage of convulsion, for it is upon this that the hypothesis of the direct action of $CHCl_3$ on nerve-centres mainly depends.

But before we can conclude that there is a

causal nexus between the so-called convulsion and stimulation of the spinal centres, it is necessary to exclude, 1, the presence of another possible cause or causes of muscle-phenomena operating simultaneously with $CHCl_3$; and, 2, the absence of the convulsion in any instance of the Rapid Method of Induction.

Now, during the sub-stage of convulsion, consciousness is not as yet lost. There is, therefore, the possibility of the exercise of volition, which may be manifested by struggling. Besides this causal factor, which is present, and may or may not be in operation, there is another cause of muscle-phenomena which is both present and operating—viz., the rapid deoxygenation of the blood.

The production of muscle-rigidity by the latter is not immediate but rapidly progressive. During the interval in which it is attaining its maximum degree, it may be associated with irregular muscle-movements. Consciousness is lost immediately before or at the onset of complete muscle-rigidity. Complete muscle-rigidity may be represented by the accidental form of opisthotonos.

But the so-called clonic-convulsion is not invariably associated with the Rapid Method. On the other hand, the rapid increase of, ending

in complete, muscle-rigidity is an invariable accompaniment of it. Unless, therefore, it be proved that the development of that particular character of the muscle-phenomena, upon which is based the specific nature of the $CHCl_3$-convulsion, is prevented by the influence of some superior agency, the conclusion will follow that it does not proceed from the action of $CHCl_3$ on the spinal centres. For if $CHCl_3$ acts directly on these centres, the convulsion must be an invariable concomitant of its action (provided that the degree of it is sufficient, and it is assumed to be so), otherwise the effect of $CHCl_3$-action on them will be irregular.

There is, however, a cause to explain muscle-rigidity—viz., rapid deoxygenation of the blood, the results of which exactly correspond to those appearing in the course of the rapid induction of unconsciousness. And, in addition, there is an occasional cause—viz., volition—to explain the occurrence of occasional movements which, instead of being regarded as complex in their causation, were assumed to be derived from a single source—viz., stimulation of the spinal centres.

Thus, if voluntary movements do not concur with an abnormal condition of the muscles, there will be no clonic convulsion; and if there

be no rapid deoxygenation of the blood, there will be no muscle-rigidity, if volition and the rapid increase of CO_2 in the blood be the actual factors in the causation of the muscle-phenomena that are associated with the Rapid Method. But the Rapid Method occasions a temporary interruption to the function of aeration, which is followed by rapid deoxygenation of the blood. It does so through a displacement of air which constitutes the negative action of $CHCl_3$, and tends to diminish the rate of the absorption of $CHCl_3$-vapour into the blood. Thus, the Rapid Method is associated during the stage of muscle-phenomena, not with the physiological, but with the negative and also the physical, action of $CHCl_3$, the latter being evidenced by the reduction of the range of respiratory movements, and occasionally by their temporary arrest.

If, now, we substitute the Graduated for the Rapid Method—*i.e.*, a method that does not complicate the action of the respiratory machine, but allows of the development of simple physiological results for one that conceals them—we find a difference in the results in the absence of muscle-phenomena. Thus, the absence of, 1, the incentive to struggle, and, 2, the $+CO_2$ factor, is associated with the absence of muscle-phenomena.

It follows, therefore, that the physiological action of $CHCl_3$ does not directly cause those muscle-phenomena which are described as clonic convulsion and tonic spasm; but they occur in the course of the rapid induction of unconsciousness, with $CHCl_3$ as the agent. How does the agent operate? By rapidly displacing air in the air-way. Two consequences follow upon this result: 1, voluntary struggling, which proceeds from the feeling of suffocation produced by a respiratory overdose; 2, rapid deoxygenation of the blood. Now, the results of minus aeration in these circumstances are not due to the physiological but to the negative action of $CHCl_3$. And the origin of the fundamental error which ascribes muscle-rigidity as a pure negative result to the physiological action of $CHCl_3$, is thus traced to a fault which is inherent in and characteristic of the Rapid Method.

§ 54. *The normal course of induction.*—The simplest means of administering $CHCl_3$ is with a twofold piece of lint, cut into a certain shape, and turned into a half cone, so that when placed on the face, with the apex at the top of the nasal ridge, all communication with the external air is shut off, with the exception of the base, which remains permanently open, but the area of which may be enlarged or diminished according to the

exigencies of varying conditions. By means of this arrangement and the gradual increase of the quantity of $CHCl_3$, the proportion of the latter in the $CHCl_3$-air atmosphere may be raised so gradually as to be imperceptible to the patient. Besides this, there is the further advantage in that, after the induction of anæsthesia, a practically constant $CHCl_3$-air atmosphere may be maintained, which, for a period that varies with the strength of the $CHCl_3$-air atmosphere, will be associated with constant results. It admits, therefore, of the ready adjustment of the $CHCl_3$-constituent of the mixed atmosphere to the several requirements, not only of the law of diminishing resistance, but also of variations of the action of the respiratory machine that are consequential upon complications when they occur, as they do occasionally, in the course of anæsthesia. From the fact that the anæsthetic percentage of $CHCl_3$ becomes, after a period of action, a relative overdose if continued beyond that period, and also because of the occasional occurrence of moderate degrees of the action of complicatory causes, not necessitating the withdrawal of $CHCl_3$, all systems or apparatus stand condemned which do not contain within themselves the requisite means of regulating the proportion of $CHCl_3$ in the

$CHCl_3$-air atmosphere, both to the constant and temporary variations which appear in the progress of its action.

The first phenomenon to appear in the course of the induction of anæsthesia by the Graduated Method is, 1, an increase in the frequency of respiration. The degree of increase rises with, and is proportioned to, each successive addition to the proportion of $CHCl_3$. And in the course of the progressive increase in its frequency, 2, the action of the respiratory machine tends to become regular. These two tendencies—viz., to increase in frequency and to regularity of action—continue until the maximum strength of the $CHCl_3$-air atmosphere is reached, when they cease consequently upon the action of the respiratory machine attaining its highest frequency and becoming regular. These two characteristics are maintained by the constant action of the maximum $CHCl_3$-air atmosphere until, 3, the pupil begins to contract, when the maximum is reduced to the minimum $CHCl_3$-air atmosphere. The process of contraction gradually but progressively continues during the action of the latter (which is the anæsthetic $CHCl_3$-air atmosphere for the first periods), until, 4, the pupil becomes finally contracted (or pin-point). Simultaneously with the appear-

ance of the contracted pupil, 5, a sudden break in the character of the action of the respiratory machine occurs. Its movements become perceptibly increased in range, and may be attended with slight noise, while at the same time they become absolutely regular both as to range and rhythm—*i.e.*, the action of the respiratory machine is automatic. Automatic respiration is the fundamental sign of the state of unconsciousness. The contracted pupil is the measure of the lowest degree of unconsciousness induced by $CHCl_3$—*i.e.*, anæsthesia.

Thus, 1, there is no alteration in the complexion, which remains of its natural colour throughout, and the pulse, after the onset of automatic respiration, shows but a very slight increase in frequency, being, in normal instances, 73 in man and 75 in woman; and, 2, there is no complication of the action of the respiratory machine.

The state of sleep, however, may intervene in the course of the induction of anæsthesia. In this contingency both automatic respiration and the contracted pupil will appear earlier than normally. The appearance of these phenomena in these abnormal circumstances might lead to the conclusion, but erroneously, that the mental functions are artificially suspended. To avoid

this mistake it will be necessary to differentiate between natural and artificial sleep.

In the former, $CHCl_3$ acts as the determining causal factor; in the latter, as the sole cause. The effect of $CHCl_3$ is thus, in so far as its degree is concerned, different in them, the difference being discernible in the degree of respiratory frequency, which is greater in $CHCl_3$-anæsthesia than in natural sleep, occurring in the early stages of $CHCl_3$-action. Besides, the early appearance of automatic respiration (and of the contracted pupil) is associated with the use of a much less quantity of $CHCl_3$ than is known to be requisite for the production of anæsthesia. Thus, the contracted pupil, when it occurs early, is not a $CHCl_3$-result. And seeing that all the results of $CHCl_3$-action, with the single exception of the sluggish dilated pupil, may be severally caused by different agents acting simultaneously with it, it becomes essential to ascertain, in the first place, whether the degree of $CHCl_3$-action is sufficient to explain, the sluggish pupil excepted, any given phenomenon occurring during its progress. For if $CHCl_3$ can be excluded, the study of its causation will consequently be made simple; while, on the other hand, if $CHCl_3$ cannot be excluded, the question to decide will be,

Does $CHCl_3$-action cause it in this particular instance?

§ 55. *Abnormal phenomena appearing in the course of induction.*—Familiarity with the normal course enables us to detect abnormalities which may complicate it. These are divided into, 1, deviations from, and, 2, complications occurring during, this period of $CHCl_3$-action. Deviations from the normal course are due either to, 1, excess; or, 2, deficiency of the $CHCl_3$-constitutent.

1. The characteristic phenomenon in the former is the early appearance of duskiness. Its origin is either in a too rapid increase of the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere, or, where the normal method is applied, in the presence of some abnormal condition of the respiratory machine—*e.g.*, nasal stenosis or a slight degree of emphysema, which is unknown, or if known, not accurately gauged.

2. Delay at any point in the transitional period between consciousness and unconsciousness is, in the case of the nervous, associated with an increase in the degree of pallor. Its origin is either in too gradual an increase in the proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere, or, if the normal method is applied, in $CHCl_3$ being below the standard strength.

Complications occurring in the normal course

of the induction of anæsthesia are, 1, mechanical obstruction in the air-way resulting from displacement of the base of the tongue. Its characteristic is lateness of the occurrence of duskiness. It is an indirect result of $CHCl_3$-action, and is invariably associated with some predisposing condition, such as an abnormally large tongue, or debility of its muscles; 2, voluntary inhibition of breathing, determining a temporary respiratory overdose; 3, voluntary arrest of the action of the respiratory machine, which may occur at any stage in the course of induction, and is occasionally the last act of consciousness; 4, reflex arrest of the function of the respiratory centre by direct stomachic action, frequently appearing in instances where there has been no preparation—*e.g.*, in accidents; and 5, complete closure of the glottis, through a floating polypus becoming impacted in it.

Some of these complications, unless counteracted, progress in intensity, and from small beginnings lead to critical results. It is necessary, therefore, to exercise a constant watch upon the course of $CHCl_3$-action in order to detect the earliest appearance of abnormal signs. Their cause can thus be isolated with the least possible difficulty, and may either be put out of opera-

tion, or, when that is impossible, its results placed in the most favourable circumstances to their natural disappearance. Thus, if excess of $CHCl_3$-vapour in the air-way be the sole complicatory agent, its removal will be followed by the return to the normal state. But the converse is not necessarily true—viz., that if the amount of $CHCl_3$ be deficient, its increase to the normal will be followed by the return to the normal, for the reason that the state of the respiratory machine may be such as to determine the temporary cessation of $CHCl_3$-administration during partial consciousness.

Again, if mechanical obstruction be the sole cause of duskiness, the removal of $CHCl_3$ will not be followed by its immediate and complete disappearance, though there will be a diminution of its intensity, due to the displacement of the $CHCl_3$-air atmosphere by air. But it will begin to disappear immediately after the removal of its ultimate cause—viz., the abnormal position of the base of the tongue.

But in the instance of emphysema, the removal of $CHCl_3$ will be followed by an increase of the intensity of duskiness, on the supposition that the graduated method is not adapted to the abnormal condition, owing to the inability of congested abnormal lungs to unload themselves

with normal rapidity. In this contingency the rational treatment will consist in ensuring the normal patency of the air-way.

Thus, in the case of duskiness, considered generally, the removal of $CHCl_3$ may be followed by one of three different results—1, its immediate and complete disappearance; 2, its continuance with a slight decrease of intensity; and 3, its continuance with a progressive increase of its intensity. And, as in the case of the contracted pupil, so of duskiness, it will be essential to demonstrate that $CHCl_3$ is acting in a sufficient degree to cause duskiness before it be concluded that all instances of duskiness are invariably the result of $CHCl_3$-action.

In the more severe forms of complication—*e.g.*, respiratory arrest associated with mechanical obstruction after the removal of $CHCl_3$—the rational treatment is, 1, to ensure the normal patency of the air-way; and, 2, to expel artificially its contents, if there be any doubt as to the presence of a relative excess of $CHCl_3$ in them. This procedure tends to diminish the retardation of the alveolar circulation, and consequently leads to the progressive reduction of the congested lungs.

§ 56. *Reduction of the dilated pupil.*—It may happen that the normal degree of unconscious-

ness is exceeded—*i.e.*, instead of anæsthesia, some degree of narcosis is induced. This abnormal result may be due either to initial error in the maximum amount or failure in diminishing the latter to the minimum when the pupil begins to contract. But whenever the state of narcosis is present, it is of the first importance to reduce it to that of anæsthesia before the commencement of the surgical operation. For if a complication of reflex origin supervene early, $CHCl_3$ will be acting in a degree—the anæsthetic—which is favourable to its natural progress, whereas a narcotic degree of $CHCl_3$-action opposes, according to its degree, a greater or less obstacle to it.

If the pupil be more or less widely dilated, the $CHCl_3$-air atmosphere is to be removed and replaced by air until a sensible diminution of its size is effected, when $CHCl_3$ is again introduced, but in the smallest proportion—viz., one drop. As the pupil tends to contract the proportion is increased, the object being to reduce the pupil gradually so as to avoid a return to consciousness. Thus, when the pupil is finally contracted, the proportion of $CHCl_3$ reaches the normal—viz., the minimum to which it would have been reduced had no fault been committed.

If the pupil be moderately dilated the with-

drawal of $CHCl_3$ is not necessary, but its amount is at first to be reduced proportionately to the degree of dilatation, and afterwards gradually increased as the tendency to contraction is manifested.

In the foregoing examples the dilated and sluggish pupil is associated with duskiness and obstructed respiration. And as the pupil tends to contract, so do the latter tend to become normal.

But the state of anæsthesia—*i.e.*, automatic respiration and normal colour of the blood—is attained in some instances, and yet the pupil is found to be widely dilated but always sensitive. The occurrence of this abnormal phenomenon might offer additional evidence of the irregularity which is assumed to be characteristic of the results of $CHCl_3$-action, on the false ground that, because it appears during its progress, therefore it is caused by it. But as matter of fact, the appearance of the sensitive pupil proves that the relation between $CHCl_3$ and the contracted pupil is not an intimate one. For it may, as on these and also other occasions, be interrupted. The inference, therefore, necessarily follows that another agent exercising a more powerful influence on the pupil than the anæsthetic degree of $CHCl_3$-action is simul-

taneously operating with the latter when dilatation occurs.

Those who manifest more than the usual degree of "fear" in the course of induction, present, at the onset of automatic respiration (always excluding complication of the respiratory machine), a widely dilated pupil. The dilatation continues for a definite period—ranging from 50″ to 2′—at the end of which it is followed by immediate return to the contracted state. (These instances are to be anticipated and observation concentrated on the pupil, else the sudden change will pass unnoticed.) The explanation of this interesting phenomenon is as follows: the emotion of fear, in its higher degrees, is associated with extreme dilatation of the pupil, and its results remain up to and after the onset of anæsthesia. For the lower centres, through which the higher—viz., the cerebral—act upon the several functions of the organism, continue in a state of disturbance for some period after their cause ceases to operate on them. In other words, when the mental functions are suspended, those of the lower centres—viz., the cardio-inhibitory and vaso-motor, which have been directly or indirectly affected during consciousness—continue in a state of abnormal activity for an interval

corresponding to the degree of disturbance to which they had been subjected before the onset of unconsciousness. Dilatation of the pupil is associated with the abnormal activity of both these centres. And on the return to their normal state, which begins to take place immediately after the removal of the disturbing factor, the pupil, no longer influenced by their agency, returns immediately to that condition, which is determined by the sole cause now in operation — viz., the anæsthetic degree of $CHCl_3$-action.

A second group, in which the pupil is dilated at the onset of anæsthesia, is characterised by the following causal conditions: 1, extreme emaciation; 2, high fever; and 3, depressant results of pain.

This form of the dilated pupil, which may be termed the "sensitive pupil," in contradistinction to the sluggish dilated pupil of $CHCl_3$-narcosis, presents a tendency to diminish gradually and progressively in size in the course of anæsthesia. Thus, after a period varying from 10′ to 20′, it finally becomes normally contracted, and remains so until the termination of $CHCl_3$-action. The factors which apparently are concerned in its causation are — 1, reduced vitality of the tissues,

arising from impaired nutrition; and 2, their abnormal sensitiveness to slight alterations in the constitution of the blood, induced by $CHCl_3$. But the tissues, which at first resent a change in their nutritional surroundings, afterwards adapt themselves to it in the course of its continuance, by virtue of their inherent power of resistance against adverse influences.

§ 57. *Causation of the abnormal phenomena occurring in the induction of unconsciousness.*—The chief of these are—I., dilatation of the pupil; II., arrest of respiratory movements; and III., failure of the pulse.

I. The dilated pupil may be associated with the natural colour of the complexion or with duskiness. In the former there are three varieties: 1, the sensitive pupil; 2, product of emotion; and 3, of returning consciousness in those instances in which the pupil becoming contracted, not as the result of $CHCl_3$-action, but through the intervention of sleep, its significance is misinterpreted, and the amount of $CHCl_3$ is, as the consequence of error, reduced. In the latter there are also three varieties: 1, the sluggish pupil of narcosis, which contracts gradually on the withdrawal of $CHCl_3$; 2, the sensitive pupil of the later stages of intervening mechanical obstruction, which rap-

idly contracts to the normal after its removal. These two examples show the different degrees of the same effect which $CHCl_3$ and obstruction in the air-way exert respectively upon the blood; and 3, a complex variety resulting from the combined operation of $CHCl_3$ with mechanical obstruction. In it the removal of obstruction is followed by rapid diminution of the size of the pupil, but it does not reach normal contraction. The lower degree of dilatation corresponds to the degree of narcosis. The difference between the higher and the lower degrees represents the indirect result of obstruction through the deoxygenation of the blood.

II. Arrest of the action of the respiratory machine may occur with the use both of the rapid and graduated methods. In the former, it is due either to an absolute respiratory overdose alone, or to a combination of that factor with voluntary inhibition of the breathing. Mechanical obstruction may also intervene and co-operate with these factors.

Arrest—voluntary or functional—of the activity of the respiratory centre is likewise a cause. It may be accompanied by a respiratory overdose. When it is so, the progress of a natural function will be interrupted, and the

interruption thus effected may be the starting-point of a false inference respecting the action of $CHCl_3$.

The graduated will become a relatively rapid method, if it be not adjusted to the requirements of initial respiratory or pulmonic abnormalities—*i.e.*, if it produces a respiratory overdose.

In the initial normal state of the respiratory machine complications may occur at indefinite points of time during induction, arising from voluntary inhibition or mechanical obstruction, or both combined. The normal proportion of $CHCl_3$ in the $CHCl_3$-air atmosphere will become abnormal at those points of time relatively to the change in the state of the respiratory machine. And the consequence of the altered relationship between the $CHCl_3$-air atmosphere and the respiratory machine will be perceptible in the presence of a relative respiratory overdose, which will increase in degree of intensity, slowly or rapidly, according to the less or greater intensity of the complicatory factor, and will become eventually the determining factor in the complex causation of respiratory arrest.

Voluntary arrest of the action of the respiratory centre may occur, uncomplicated, in the

course of normal induction, as also its functional arrest. Under normal conditions these natural complications pursue their progress undisturbed.

Thus respiratory arrest may be either of simple or complex causation. It may occur either during anæsthesia or narcosis. Confusion originating in a prejudiced treatment of this part of the problem disappears when, 1, all the phenomena present at the onset of respiratory arrest are recorded; and, 2, all the causal factors, if there be more than one, are isolated, and proved not only to be present at the time, but also in operation, by phenomena which characterise their action.

III. Failure of the pulse occurring in the course of induction is invariably consequent upon cardiac syncope.

Cardiac syncope presents two forms, the primary and secondary.

Primary syncope is invariably associated with some defect of the cardiac tissue. Three instances of it occurred during the early stages of induction. They presented a predisposing factor in intense emotion. Three also occurred near to the onset of anæsthesia. But in these there was no complication of the respiratory machine consequent upon emotion. In all the

action of the respiratory machine continued for a definite period after the heart had ceased to functionate.

Secondary cardiac syncope may follow upon arrest of respiratory movements, and will do so if the source of obstruction (which is either present at the onset, and is the cause of the complication, or appears subsequently) is not removed within a given interval. The pulse fails as the result of temporary cardiac exhaustion. But the abnormal condition of the heart is not to be regarded as synonymous with its complete failure, nor as being of superior importance to respiratory obstruction. For it is simply a secondary phenomenon resulting from pulmonic congestion which accompanies or follows upon respiratory arrest. The removal of the ultimate cause will be followed by the disappearance of all the results which are directly or indirectly dependent on it. Thus the removal of the cause of respiratory obstruction will be followed by the progressive disappearance of pulmonic congestion. And the removal of the latter will be followed by the return of the pulse.

§ 58. *The pupil not available.*—The eyes may be absent, or the seat of disease or deformity preclude the use or the view of the pupil. The pupil is contracted by opium, and dilated

by atropin. It is contracted in ataxia. In all these contingencies the measure of the anæsthetic degree of $CHCl_3$-action is confined to the normal colour of the blood.

The contracted pupil is selected in normal conditions as the measure of the anæsthetic degree of $CHCl_3$-action for practical purposes. It is easy of access, and slight variations in its size are more readily observed and differentiated than corresponding variations of the colour of the blood. But its relation to $CHCl_3$-action is not so intimate as that of the blood. Thus the effect of $CHCl_3$ on the blood cannot be prevented. But the indirect effect of $CHCl_3$ on the pupil is prevented by atropin and by the higher degrees of mechanical obstruction to breathing.

§ 59. *Standardising $CHCl_3$-action, period of induction.*—The isolation of the parts on which $CHCl_3$ acts, leads in practice to the prevention of its physical action, and in investigation to the determination of the influences they respectively exert when their conditions are abnormal. For this purpose, seeing that the results of $CHCl_3$-action vary according to its degree, it is requisite to preserve the same rate of rapidity in the action of the cause—*i.e.*, the $CHCl_3$ constituent in the $CHCl_3$-air atmosphere is to be

increased regularly and uniformly. When the initial conditions of the respiratory machine and blood are normal, the progress of normal $CHCl_3$-action is invariably followed by the succession of the same phenomena. If, therefore, any variation appears in one or more of these, or if some collateral phenomenon intervenes, it will be capable of being easily isolated and traced to its cause. Thus the distinction between $CHCl_3$- and non-$CHCl_3$-results is effected.

The failure in differentiating between the physical and physiological action of $CHCl_3$ and between the results of $CHCl_3$ and those of other causes acting simultaneously with it leads to false conclusions. For example, $CHCl_3$ is administered by the Rapid Method, which favours its physical action. Voluntary inhibition is supposed to supervene, and to be accompanied by mechanical obstruction in the air-way. The resultant state will consequently be complex. But during its progress respiratory arrest is supposed to occur, the attendant phenomena being, 1, dilated pupil; 2, cyanosis; 3, venous distension; and, 4, diminished frequency and increased strength of the pulse. What is the cause of arrest? Is it due to the direct action of $CHCl_3$ on the respiratory centre? Or is it

due to an abnormal condition of the respiratory machine, the result of a cause acting on one of its component parts?

Before the former is concluded, it is necessary to demonstrate that the latter is inefficient to produce arrest. The jaws, therefore, are to be forced apart, the base of the tongue replaced in its normal position and maintained in it, and the contents of the air-way artificially expelled. Thus both respiratory overdose and mechanical obstruction will be removed. But, following upon their removal, the action of the respiratory machine will be spontaneously resumed. The removal of these two possible causes proves, therefore, that the respiratory centre is not primarily affected in this supposed instance. But the conclusion is not to be drawn from this and similar instances that in a complicated state of the respiratory machine the respiratory centre is always normal when arrest takes place. For voluntary arrest of its action may conceivably occur during cyanosis resulting from respiratory overdose, accidentally induced in the initial stages of $CHCl_3$-administration.

Where causation is complex, it will be necessary to analyse the compound cause into its simple factors, as in the example which has just been recorded. Different degrees of action of

the several causal factors will be associated with differences in the intermixed results, and will, therefore, explain the irregularity which is characteristic of them.

Where causation is simple, but the result—*e.g.*, arrest of respiratory movements—may be produced by different causes, it will be necessary to know the mode of operancy of each possible cause—*i.e.*, the characters of the phenomena accompanying it, and the course which they pursue. Thus differences in the mode of onset of respiratory arrest—rapid, sudden, or gradual—will indicate the several sources from whence it proceeds.

Where the contingency may exist of two or more causes acting simultaneously, one of which is $CHCl_3$, it will be necessary to render the results of the latter constant (for it is the only cause over which control can be exercised) in order to be able to estimate the results of the others—*i.e.*, $CHCl_3$-action is to be gradually raised to the anæsthetic degree of action by a method the successive stages of which are known to be associated with uniform results. If, then, respiratory arrest occurs during any one stage, instead of inferring that $CHCl_3$ is the cause of it, on the assumption that the arrest is a simple phenomenon proceeding from an

abnormal condition of the respiratory centre, the inquiry will be, "What is the cause of it?" To this end it will be necessary, first of all, to remove the results of those causes which are present and known to affect the action of the respiratory machine. If respiration is spontaneously resumed after these causes have been put out of operation, and their results, where necessary, artificially removed, the second stage of the inquiry will be reached—viz., the relation of $CHCl_3$ to the causation of respiratory arrest. Was $CHCl_3$ the only cause in operation at the time of its occurrence, or was it associated with other causal factors? In the latter contingency $CHCl_3$ may or may not be causally related to respiratory arrest. But if the fact is established that $CHCl_3$ is a causal factor, we can next proceed to the third stage of the inquiry, "How did $CHCl_3$ cause if acting alone, or help to cause if associated with mechanical obstruction, arrest of the action of the respiratory machine?"

If respiration is spontaneously resumed after, 1, rendering the air-way normally patent (and keeping it so), and, 2, removing its contents, the conclusion will follow that the causation of arrest is dependent upon the factors which have been put out of operation—viz., respiratory overdose and mechanical obstruction. And the

arrest is thus partially the direct result of the physical action of $CHCl_3$.

If, on the other hand, spontaneous respiration does not immediately follow upon the removal of respiratory overdose and mechanical obstruction, but is resumed after the application of artificial means, the conclusion will follow that another causal factor (or factors) has been predominant in the causation of arrest. These factors are — 1, pulmonic congestion; and 2, exhaustion of the respiratory muscles. An abnormal condition of the respiratory centre is excluded by the reappearance of respiratory movements and their return to the normal within a comparatively short interval, the length of which is determined by, 1, the degree of pulmonic congestion; and, 2, that of muscular exhaustion. The longest, which is not more than 75″, cannot be adduced as valid evidence of a depressed condition of the centre, supposing that in this respect the respiratory centre follows the ordinary rule—viz., that disturbance directly effected in a nerve-centre by the periodic action of an agent continues for a considerable time before it completely disappears.

In the case of pulmonic congestion, as also of exhaustion of the respiratory muscles, $CHCl_3$ acts both indirectly and negatively. Pulmonic

congestion may be induced rapidly or gradually. In the former contingency, it is the chief factor in the causation of respiratory arrest; in the latter, the increased amount of work done by the muscles of respiration, combined with an abnormal blood-supply, leads, if uncounteracted, to their temporary exhaustion, which thus becomes the determining factor.

These factors—pulmonic congestion and muscular exhaustion—represent successive stages in the course of the progressive negative action of $CHCl_3$, during which its physical action is of secondary import in the causation of respiratory arrest. But the latter may, under certain conditions, play the chief or the sole part in it. And in addition, mechanical obstruction is to be included as an independent and possible auxiliary factor. Thus a cause other than the depressant action of $CHCl_3$ on the respiratory centre, or combination of causes, may be present and operating at the time when rapid or gradual arrest of respiration occurs. And the differences in the progress of the antecedent phenomena and in their respective degrees at the onset of arrest will be explained by the different degrees of action of a single cause or by varying degrees of the component factors *where* the causation is complex. Thus in this group of instances of

respiratory arrest the investigation is diverted from the profitless task of deducing the physiological action of $CHCl_3$ from a phenomenon with which it is not causally related. But there is another group of instances of respiratory arrest occurring in the course of the induction of unconsciousness, and characterised by suddenness of onset. Sudden onset of respiratory arrest is caused in one of two known ways,—by an act of the will, or by abnormal stomachic action. But on the assumption that $CHCl_3$ acts directly as a depressant on the respiratory centre, a third possible cause is introduced. Sudden onset of respiratory arrest occurs either during a normal or an abnormal state of the respiratory machine. And the phenomena following immediately upon its occurrence present differences in each of those sub-groups. In the former, the complexion is either normal (subsequently becoming dusky) or pallid; in the latter, the degree of duskiness is either increased or the complexion becomes livid. Thus sudden respiratory arrest may take place under these two opposite conditions of the circulation—1, normal pulse, gradually increasing in strength and diminishing in frequency; 2, immediate fall of blood-pressure. The (assumed) physiological action of $CHCl_3$ on the respiratory centre can

only be associated with one of these conditions. Supposing, for the sake of argument, that $CHCl_3$ acts directly upon the centre, it will follow that there is at least one other cause in the group in question affecting the respiratory centre during $CHCl_3$-action. The relationship of $CHCl_3$-action to sudden respiratory arrest is thus limited. And seeing that $CHCl_3$ cannot be the cause of all instances of sudden arrest, as the hypothesis of depressant action affirms, the question may rationally be proposed, Does $CHCl_3$, as matter of fact, directly affect the respiratory centre in that sub-group of instances of respiratory arrest which, logically, may be ascribed to its action?

Examining the data from this point of view, we find that, I., the results of $CHCl_3$-action, as an assumed depressant on the respiratory centre, do not conform to the universal rule of increasing in intensity proportionately to the increase of the degree of action. For arrest of respiratory movements occurs both before and after the onset of unconsciousness. II., disturbance in nerve-centres caused by the direct agency of drugs is invariably associated with, and is the origin of, corresponding changes in neighbouring centres. The centre most intimately connected with the respiratory is the vaso-motor. The

evidence points to the occasional and not the universal occurrence of vaso-motor phenomena in respiratory arrest. If, then, $CHCl_3$ be the cause, the conclusion will inevitably follow that its action is associated with two different sets of phenomena. But this is contrary to the law of causation, viz., that a cause has always the same effect—*i.e.*, in normal conditions its results, direct and indirect, will always be the same. III., the time of the occurrence of respiratory arrest is indefinite. But this is a datum of no importance in itself. It possesses value only when the degree and kind of $CHCl_3$-action are determined. What is of importance, however, is this—in the course of the diminution of the degree of $CHCl_3$-action during anæsthesia, arrest of the action of the respiratory machine may occur at any moment. When that happens, it will, on the assumption that the depressant action of $CHCl_3$ is its cause, be perceived that there is a remarkable disproportion between cause and result—viz., that as the degree of intensity of the former diminishes that of the latter is increased; while no variation of the part affected—viz., the respiratory centre—is adduced to explain the discrepancy.

Thus, the results which are, on supposition only, ascribed to $CHCl_3$-action do not conform

to the laws of causation. But it cannot logically be inferred that the action of $CHCl_3$ is irregular or peculiar, on the ground that irregular or peculiar phenomena appear in the course of its operation. For these phenomena may possibly be caused by agents independently of $CHCl_3$, but operating simultaneously with it. It will be necessary, therefore, in the first instance, to prove that they are actual $CHCl_3$-phenomena.

But it may be objected, by those who uphold the hypothesis, that the fall of blood-pressure accompanying arrest of respiration is due to the direct action of $CHCl_3$ on the heart. Consequently $CHCl_3$, assumed to be circulating in the blood, is made to have two simultaneous effects, —one upon the respiratory centre and the other upon the heart. That conclusion is also contrary to the laws of causation. For one cause or agent can only have one effect in the particular sphere of its operation, and it may have more than one. In those circumstances, therefore, in which the action of an agent is associated with more than one result—and this is commonly the case in the human by reason of the intimate relations, both mechanical and sympathetic, between the vital functions and also between them and the pupil,—it is necessary to differentiate between

the direct result and those results which appear subsequently to it, and which are in consequence called secondary or indirect results. Now it may be argued that $CHCl_3$, always on the supposition that it exists as such in the blood, may possibly have a direct effect either on the respiratory centre or on the heart, but it is impossible that it should affect both directly.

The fall of blood-pressure accompanying respiratory arrest is, however, not universal. In those instances in which it occurs no proof is adduced, 1, that it is of cardiac origin; and, 2, that it is the consequence of $CHCl_3$-action. But assuming that cardiac failure is primary—and as matter of fact the assumption is only true in respect of a very small group of instances,—no reasons are alleged to explain the differences in the phenomena which follow upon the operation of the same hypothetical cause.

Irregularities, or, as they should properly be termed, complications, occur in the course of $CHCl_3$-action just as in that of any other agent in similar circumstances. But when the action of $CHCl_3$ is standardised, they are capable of being traced to their true sources, which are—I., abnormality of the condition of the parts affected by the several kinds of $CHCl_3$-action; and II., the intervention of collateral causes

which may be either independent of or dependent on the action of $CHCl_3$.

§ 60. *Analysis of factors: abstract considerations.*—The factors which enter into the explanation of the phenomena occurring during the induction of unconsciousness are—1, the normal method of induction; 2, the negative; 3, the physical; and 4, the physiological action of $CHCl_3$; 5, the normal or abnormal condition of the components of the respiratory machine—viz., the air-way, the lungs, and the motor-power; 6, the quantity and quality of the blood; 7, mechanical obstruction; 8, volition—inhibition and arrest of the action of the respiratory centre; and 9, functional arrest of the respiratory centre, subservient to the abnormal condition of the stomachic function.

If, now, we take an initial narrowing of the air-way—*e.g.*, nasal stenosis or naso-pharyngeal obstruction—and apply to it in the abstract an atmosphere containing less than the normal proportion of oxygen, we deduce, 1, difficulty in breathing, arising from a deficient supply of air to the alveolar region, and followed by obstruction to the alveolar circulation; and, 2, the direct results of the defective supply of oxygen—viz., pulmonic congestion and discoloration of the blood. But the same phenomena appear

in the course of the induction of unconsciousness, when the proportion of $CHCl_3$, the agent used in its production, is excessive. The initial respiratory obstruction may be partially counteracted by separating the lips if they are closed. But to avoid the consequences of the contributory influence of the respiratory abnormality, it is essential to adapt the rate of increase of the proportion of $CHCl_3$ to its requirement. And if this is done efficiently in practice it will be found that the abnormal phenomena of defective aeration do not appear, or if they appear, that their intensity is limited to a degree that is easily manageable.

In the case of pulmonic abnormality—*e.g.*, emphysema—the alveolar circulation is more sensitive to a diminution in the proportion of air in the abnormal atmosphere breathed than it would be if the lungs were normal. If, therefore, it be necessary to abstract some of the normal volume of air, as it is in the ordinary administration of $CHCl_3$, the rate of its withdrawal will be associated with less disturbance to the alveolar circulation, if it be gradually effected, than in the case of its rapid removal. But there is another factor which may intervene and affect the action of the respiratory machine in the intermediate period between conscious-

ness and unconsciousness. For the will may be stimulated to action by the feeling of suffocation which arises from the deficiency of air. Voluntary action may take the form either of inhibition of breathing and contraction of the muscles of the lower jaw, or arrest of the action of the respiratory machine. If, therefore, the function of the respiratory centre is voluntarily arrested during or antecedent to the onset of unconsciousness, and the air-way is, immediately after its occurrence, rendered normally patent and relieved of its abnormal contents, spontaneous respiration will not be resumed until the results of the disturbance in the centre disappear. On the other hand, if voluntary arrest does not complicate the abnormal state of the respiratory machine, respiration will be immediately resumed, though with different degrees of activity according to the different degrees of obstruction to which it has been subjected, when the air-way is rendered normally patent and its contents artificially removed. Now these two attitudes of the respiratory machine actually occur in the experience of $CHCl_3$-administration.

When pulmonic congestion is induced in abnormal lungs, a longer time is needed, as compared with normal ones, for its reduction. If the degree of congestion is intense, it is possible that

the heart's action may fail temporarily, through exhaustion, resulting from increased work which is necessitated by the obstacle which it endeavours to overcome. In such a contingency the cardiac failure will be secondary, not primary; and it will not be associated with complete absence of contractions as in the latter. If, therefore, during this interval of temporary exhaustion of the heart—secondary cardiac syncope—its cause, viz., pulmonic congestion, is removed, the surrounding conditions will be rendered favourable to the recovery of its normal function. But this is exactly what takes place in one group of instances of respiratory arrest. The pulse fails after the arrest of the action of the respiratory machine. There is evidence of the presence of pulmonic congestion. Spontaneous respiration follows upon its reduction, and is itself followed by the return of the pulse.

A heavy atmosphere, when it is of sufficient weight to impede the act of respiration, is the cause of the progressive expansion of the chest. It, therefore, tends to arrest the action of the respiratory machine by opposing greater resistance to the expiratory muscles than they are able to overcome. The removal of this cause, at any stage of its operation, will be

followed by the return of normal respiration. Expansion of the chest may occur, as an abnormal phenomenon, in the administration of $CHCl_3$. When it does so, it is invariably associated either with a reduction of the range of respiratory movements, or with their arrest. In both instances the removal of the heavy $CHCl_3$-air atmosphere in the airway is followed by the return to normal respiration.

Functional arrest, at the end of a full inspiration, is the antecedent requisite to the act of vomiting. If any cause intervenes and prevents full inspiration, arrest of respiration will occur during its progress, but it will not be followed by the expulsion of the contents of the stomach. For example, the mouth is supposed to be opened widely by a gag immediately before the onset of anæsthesia; but if it chance that the third stage of stomachic disturbance, viz., the act of vomiting, coincides with a given degree of respiratory obstruction, a full inspiration will be impossible, and sudden arrest of respiration will consequently take place during the act of inspiration, the complexion at the same time becoming pallid. But the obstruction, instead of being induced by mechanical means, artificial or natural, may be caused

by a temporary excess of $CHCl_3$ in the air-way—*i.e.*, a respiratory overdose. In all these instances, the immediate removal of the obstacle impeding full inspiration will be followed by, 1, sudden arrest of respiration at the end of full inspiration; and, 2, the expulsion of the stomachic contents. And this is what is found to occur in practice.

Voluntary arrest of breathing may appear at any stage during the transitionary period between consciousness and unconsciousness. It may chance that it coincides with the onset of unconsciousness. An interval will then elapse before the resumption of spontaneous respiration, and in the course of it the function of aeration will be increasingly impeded. If the state of the respiratory machine be normal when arrest occurs, duskiness will supervene and gradually increase, and subsequently disappear on the return of respiration. But if the state of the respiratory machine be abnormal, the intensity of duskiness (which is already present) will be increased, and the returning movements of respiration—on the supposition that the air-way is maintained normally patent during the complication—will be opposed by, 1, physical obstruction in the air-way; and, 2, some degree of pulmonic con-

gestion; consequently the function of aeration will continue to be impeded. Suppose, however, that during the interval the state of the respiratory machine is rendered favourable to the transit of air to the alveoli, by restoring the normal patency of the air-way and removing its abnormal contents, the return of respiratory movements will be followed by increased aeration. And this is what takes place when the excess of $CHCl_3$ is removed from the air-way in instances of voluntary arrest occurring under the abnormal condition of duskiness.

The respiratory machine presents different attitudes, after the expulsion of the contents of the air-way, in respiratory arrest. Thus, respiratory movements are in some instances immediately resumed; but in others no movement occurs. Now it is not to be inferred that, because the respiratory machine remains inactive, immediate resort to artificial respiration is necessary. For there are two possible causes of respiratory inactivity in the latter contingency—viz., severe degree of pulmonic congestion, and the continuance of the disturbance induced in the respiratory centre by volition. It becomes essential, therefore, to differentiate the instances which require artificial respiration from those which naturally

recover. If the pupil rapidly contracts, and the degree of duskiness diminishes (the air-way being normally patent, air is increasingly diffused into the alveolar region), there will be no need for the application of artificial measures. But if the pupil remains widely dilated, and no obvious change takes place in the colour of the complexion, artificial respiration will be indicated, and should be immediately applied.

Difficulty is sometimes presented by the rigidity of the jaw muscles in separating the teeth in order to replace the base of the tongue in its normal position, during which procedure rapid deoxygenation of the blood will ensue. But after it has been effected, spontaneous inspiration is supposed to be followed by a second arrest of the action of the respiratory machine. This is an example of relative apnœa. It is associated with, 1, the contracted pupil; and, 2, rapid diminution of the degree of duskiness: and it leads to the inference that the chief factor in the resulting state of complication is $+CO_2$. The function of the respiratory centre will be resumed when the proportion of oxygen in the blood becomes insufficient for the wants of the organism. And in order that the respiratory machine may respond to the stimulation of the respiratory

centre with the greatest possible result, under conditions which remain as yet abnormal, it will be essential to maintain the normal patency of the air-way until recovery is complete.

§ 61. *Difficulties encountered in the solution of the $CHCl_3$-problem.* These are, 1, the variant degrees of action of the agents which may be in operation at the onset of any given phenomenon; 2, variant degrees of abnormality in the parts affected by $CHCl_3$; 3, plural causation; 4, the same phenomenon has different causes; and 5, a given phenomenon may be indirectly, not directly, caused by $CHCl_3$.

In order to arrive at the phenomena associated with the physiological action of $CHCl_3$, we have to exclude the results of its negative and physical actions, and also those of independent causes. But the results of the physiological action of $CHCl_3$, like any other agent, vary in degree according to its degree of action. Thus there are different degrees of the abnormal condition of the cerebral centres—*i.e.*, of unconsciousness associated with different degrees of the same phenomena. The phenomena of the lowest degree of unconsciousness—*i.e.*, the state of anæsthesia—are automatic and efficient respiration, increased frequency of respiration, the contracted pupil, normal colour

of the blood, slight increase in frequency of the pulse, and muscle-relaxation.

The phenomena of the degrees of unconsciousness greater than anæsthesia—*i.e.*, of the different degrees of narcosis—are automatic but inefficient respiration, increased frequency of respiration, dilatation of the pupil, discoloration of the blood, diminution in the frequency of the pulse, and muscle-relaxation.

The inefficiency of respiration and the discoloration of the blood are due to the negative action, the inseparable associate of the narcotic degree of $CHCl_3$-action. They are not, therefore, to be regarded as evidence of difference in kind of phenomena attending different degrees of physiological action. The diminished frequency and increased strength of the pulse is a concomitant of physiologic pulmonic congestion, which is the direct result of negative action. The results which present different degrees of intensity, according as the physiological action of $CHCl_3$ is anæsthetic or narcotic, are—1, unconsciousness; and 2, muscle-relaxation. They appear, therefore, to be the nearest related to it. There can, of course, be no question that they are directly or indirectly the consequences of it. Whereas, in the case of respiratory frequency, the question, Is it

a physiological $CHCl_3$-product? cannot be affirmed with certainty from the fact that there is already a cause in operation — viz., the displacement of air by $CHCl_3$-vapour leading to impairment of the function of aeration, which is known to produce it.

It is, however, in the case of the pupil that doubt appears with regard to the physiological action of $CHCl_3$ conforming to the law that the degree of action determines the degree of result, assuming that the part acted upon remains constant. For the pupil is minutely contracted in anæsthesia, but dilated more or less in greater or less degrees of narcosis. A dilated pupil is either sensitive or sluggish to the action of light. In $CHCl_3$-narcosis it is invariably sluggish, being more or less so according to greater or less degree of dilatation. In $CHCl_3$-anæsthesia, the inference, and it amounts to certainty, is that the iris is normally sensitive. Thus, a difficulty appears in explaining the relationship of the pupil to physiological $CHCl_3$-action.

In sleep — the natural suspension of the functions of the cerebral centres—the pupil is contracted and the muscles are relaxed. The same phenomena appear in $CHCl_3$-anæsthesia, which may be regarded as an artificial sleep.

And it would appear that they are the indirect results of the suspension of the functions of those centres. But either the contracted pupil or muscle-relaxation (or both) may conceivably have another relationship to $CHCl_3$-action than that depending on the intermediate condition of anæsthesia. Such an inferential relationship will open the way to the explanation of at least the dilatation of the pupil in $CHCl_3$-narcosis, for the degree of its dilatation is directly proportioned to the degree of narcosis. But while there are different degrees of narcosis—and the abnormal condition of the cerebral centres, equally with the other components of the state of narcosis, presents differences in degree—there is only one degree of sleep. And this restriction precludes us from the knowledge of what the attitude of the pupil would be if, as is the case in artificially induced unconsciousness, there were different degrees of natural unconsciousness.

The inquiry, therefore, is for the present opposed by a very interesting question, "How does $CHCl_3$ cause unconsciousness?" Auxiliary to its solution are the following data, which will form the subject of subsequent consideration: I., in the course of the action of $CHCl_3$, beginning with the state of anæsthesia, it is found necessary, in order to maintain it, to

reduce progressively the amount of $CHCl_3$; II., some of its components undergo variations during the progress of normal anæsthesia—*e.g.*, there is increased acceleration of the pulse and respiration, and the sensitiveness of muscle to local and nerve stimulation diminishes.

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END OF THE FIRST VOLUME.

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